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The American Heart Journal

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Original Communications

SUDDEN DEATH DUE TO EXACERBATION OF LATENT SYPHILITIC MYOCARDITIS*

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THIS paper is based upon a pathological study of eight cases of sudden death, seven of which were coroner's cases, occurring in the pathological service of the University of Michigan since 1905. They all presented a form of syphilis of the heart unknown to the textbooks of internal medicine and pathology; and, as far as I can discover, this is the first reported study of a condition which is interpreted as an acute exacerbation, or crisis, of a previously latent myocardial syphilis. It differs from other syphilitic affections of the heart both in symptomatology and pathology. The latter is unique, and finds a counterpart only in experimental animal syphilis and in certain forms of congenital syphilis, notably that of the umbilical cord. In all cases histological evidences of an older latent syphilis were present, not only in the heart, but also in the aorta, meninges, liver, testes and other organs. With these older areas of fibrosis, lymphocyte and plasma cell infiltrations, there are found in these cases more or less extensive areas of more recent and more active inflammatory infiltrations in the myocardium and aortic wall made up chiefly of lymphocytes but with numerous polymorphonuclear leucocytes also present. It was the occurrence of definite areas in which the latter were predominant that led me for a long time to regard some of the earlier cases as showing a mixed infection, a secondary pyogenic infection upon an older syphilis. The absence of other evidences of a pyogenic process, and the occurrence of great numbers of spirochetes in the polymorphonuclear infiltrations especially, spoke for the pure syphilitic character of the process, but it was not until an acquaintance with the polymorphonuclear reactions of syphilis of the placenta and umbilical cord, and of experimental animal syphilis led to the

*From the Pathological Laboratory, University of Michigan.
Read before the Association of American Physicians, Washington, D. C., May, 1925.

belief that the histologically similar infiltrations of the myocardium represented an active exacerbation of the syphilitic infection alone, that the syphilitic entity of the cardiac condition was finally fully recognized. Its histological features are in every way identical with the polymorphonuclear reactions of the critical phases of experimental animal syphilis. The last three cases of the group were so striking in their extensive lesions of this nature and so wholly convincing as to the correctness of this view that the older cases were restudied, and the entire group of eight cases assembled for the presentation of this most striking pathological lesion of cardiac syphilis. The cases are given below in greatly condensed form as to clinical history and pathological protocol, only the most essential points being considered.

REPORT OF CASES

CASE I.—(Coroner's case, March, 1905) Mr. C., aged fifty-three, lawyer. The family physician at time of death had no knowledge of any syphilitic infection, but the patient's wife had had several miscarriages and the only living child was feeble-minded and presented syphilitic stigmata. On a business trip to Ann Arbor he developed very suddenly cyanosis, marked shortness of breath, intense pain in precordium extending down right arm, epigastric distress, pronounced weakness and anxiety, and died in sleep during the night. Autopsy showed a flabby dilated left ventricle with numerous light yellowish patches in the myocardium, especially toward the apex and in the septum. These were at first thought to be anemic infarcts, but the absence of any hemorrhagic border was noted. There was a distinct aneurysmal bulging of the lower portion of the left anterior ventricular wall, and the muscle of this portion was thinned and showed fibrous streaks. There were no valvular lesions. The microscopic examination showed a diffuse lymphocyte and plasma cell infiltration of the left ventricular wall, with many areas showing numerous polymorphonuclears. In these areas, a year later, spirochetes were demonstrated in great numbers. Other portions of the heart wall showed more subacute lesions in the form of fibroblastic and plasma cell infiltrations, some of which were so large as to suggest miliary gummas, while other areas presented older fibroid lesions. The coronary arteries showed relatively slight changes. No anemic infarcts found. Although to the naked eye the aorta presented but slight atheroselerotic changes, the microscopic examination showed numerous small active syphilitic lesions. Similar lesions were found in the leptomeninges, liver, pancreas and adrenals. The testes showed an advanced orchitis fibrosa syphilitica. The lungs presented the picture of a chronic passive congestion (brown induration) with an acute exacerbation and marked edema. *Pathological Diagnosis.*—Acute cardiac insufficiency. Acute pulmonary stasis and edema. Active syphilitic myocarditis. Latent syphilitic lesions in leptomeninges, aorta, liver, pancreas, adrenals and testes. Atrophy, passive congestion and acute parenchymatous changes in all organs.

CASE II.—Mr. P., aged forty-two, traveling salesman. Married; wife never pregnant. Had syphilis at 21. Prolonged course of treatment with apparent clinical cure. Fine appearing, powerfully built man of very active habits. No clinical symptoms until the day preceding death. In July, 1905, he returned from a trip on a very hot day, complaining of vague pain in precordium and of being "all in". He was slightly cyanotic. He attributed all of his symptoms to the heat; and taking a palm-leaf fan and removing his coat, seated himself in a rocking-chair on the porch, where he was shortly afterwards found dead. Autopsy at coroner's request showed a very large heart with a much dilated left ventricle. The entire

myocardium, but especially that of the left ventricle, was mottled with yellowish streaks and patches without hemorrhagic borders. His heart was a perfect duplicate of that seen in Case VIII (Figs. 1 and 2). The gross pathological diagnosis was that of anemic infarction although the absence of hemorrhage was noted. No valvular changes. The microscopic examination showed an active diffuse syphilitic myocarditis (spirochetes demonstrated later), in the form of plasma cell and lymphocyte infiltrations, with areas of polymorphonuclear infiltrations extending in cords between the heart muscle bundles. No anemic infarcts were found; and the coronaries presented no changes. Small patches of fibrosis were present in the septum, and in the plasma cell infiltrations small areas of angioblastic and fibroblastic

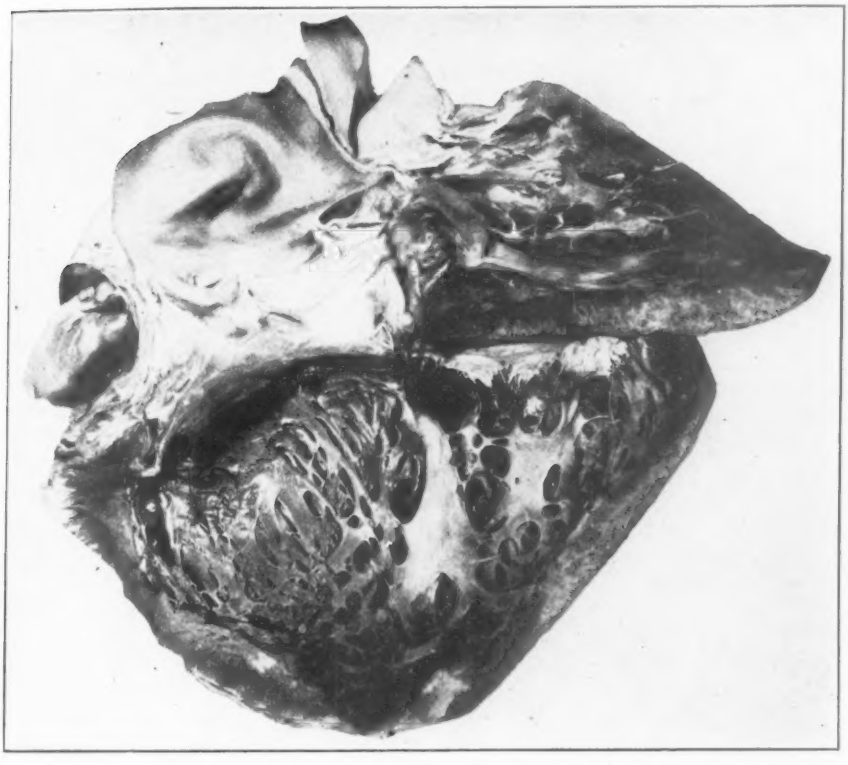

Fig. 1.—Photograph of heart from Case VIII. Acute syphilitic myocarditis. Left ventricle opened, showing marked dilatation. Myocardium at edge of incisions shows the patchy light-colored areas corresponding to the syphilitic infiltrations and granulomatous areas. The absence of hemorrhagic or congested zones about these is well shown. This photograph shows a typical picture of the condition, in one of the most marked of our cases. The heart from Case II was an almost exact duplicate of this in its gross appearances; the other cases showed less marked gross changes.

proliferations were occasionally found (miliary gummas). Active syphilitic lesions in the form of plasma cell infiltrations were found also in the aorta, liver, pancreas, adrenals and testes. The leptomeninges showed small focal thickenings. Lungs presented an intense congestion and edema. The *pathological diagnosis* was: Acute cardiac insufficiency; pulmonary congestion and edema; active syphilitic myocarditis; dilatation of left ventricle; latent syphilitic lesions in leptomeninges, aorta, liver, pancreas, adrenals and testes. Old scar on glans penis. Extreme passive congestion of all organs.

CASE III.—Autopsy J-XII, Pathological Laboratory. Mr. C. V. C., Nov. 1905. Farmer, aged about fifty-five, admitted to University Hospital with severe symptoms of acute cardiac insufficiency. No complete history. Denied venereal disease, but admitted alcoholism. Marked shortness of breath and cyanosis. Died twenty-four hours after admission. Autopsy showed localized old pericardial adhesions. The heart was dilated; on the anterior wall of the left ventricle there was an aneurysmal bulging of the size of a small orange reaching nearly to the apex. On opening the heart this was found to be filled with a red thrombus, partly old and partly recent,

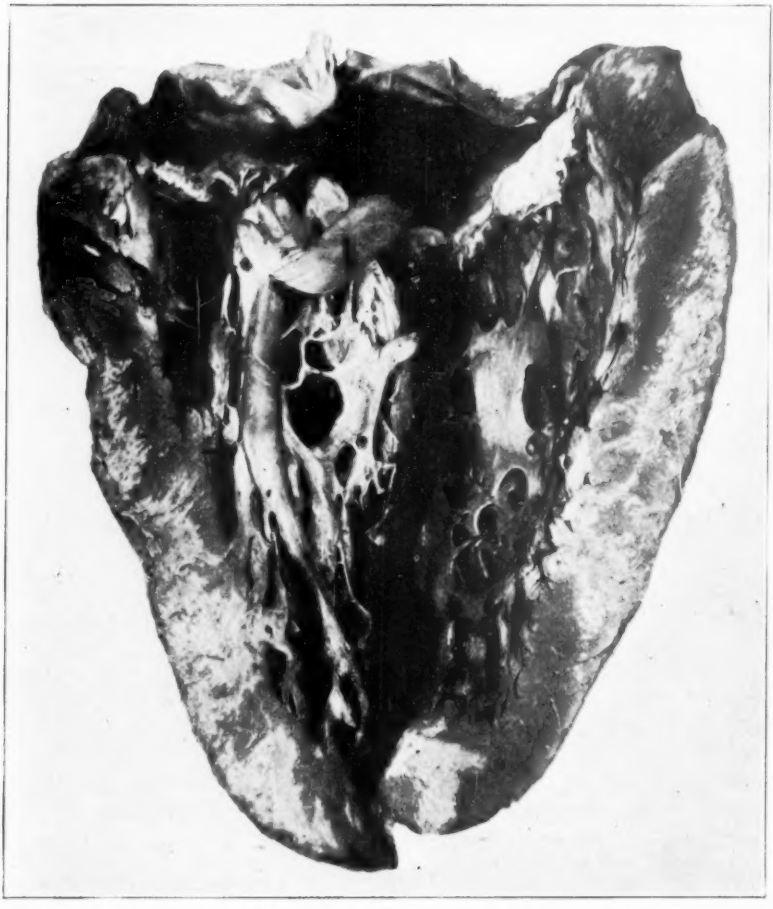

Fig. 2.—Closer view of flap of anterior wall of left ventricle from heart shown in preceding figure. This shows more distinctly the character of the light-colored patches of the syphilitic infiltrations of severe acute syphilitic myocarditis.

attached to the greatly thinned and fibrous wall of the bulging portion. In this aneurysmal wall there was almost complete absence of heart muscle. Other portions of the left ventricle wall showed numerous grayish and yellowish patches which were interpreted as fibroid patches. No infarcts and no gummas were found. The mitral valve showed a relative insufficiency; the aortic valves showed some thickening and a slight stenosis. Over the parietal endocardium there were patches of fibrosis. The coronary branches were dilated, and somewhat sclerotic, particularly the lower portion of the left anterior descending branch which was completely

obliterated over the wall of the aneurysmal dilatation. The microscopic examination showed a marked diffuse fibrosis of the anterior wall of the left ventricle and a more patchy fibrosis of the septum and posterior wall. Only traces of heart muscle could be found in the wall of the aneurysmal dilatation. The endocardium over this showed marked thickening and its surface covered with an adherent organizing red thrombus. These findings were interpreted as the result of an old syphilitic myocarditis combined with infarction due to syphilitic obliteration of the left anterior descending coronary. The other coronary vessels showed slight sclerosis. Throughout the septum and the posterior ventricular wall there were numerous active inflammatory infiltrations of lymphocytes and plasma cells with polymorphonuclear foci. In these areas spirochetes were later demonstrated. Active syphilitic lesions were found also in the aortic valve, the coronaries, wall of the

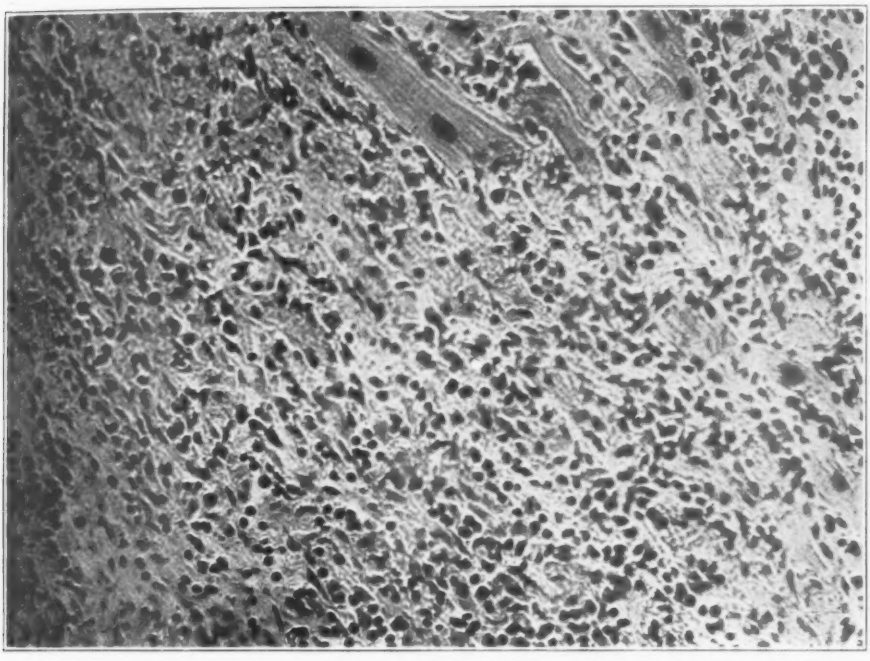

Fig. 3.—Photomicrograph of area of syphilitic myocarditis from heart of Case I. Border of large area of plasma-cell and lymphocyte infiltration and fibroblastic proliferation, with groups of polymorphonuclears. Exacerbation of latent syphilis of myocardium.

aorta, and in the testes. A large puckered scar was present upon the penis just back of the corona. *Pathological diagnosis.*—Acute cardiac insufficiency. Aneurysmal dilatation of anterior portion of left ventricle with organizing red thrombus; old syphilis of left anterior descending coronary, infarction and syphilitic fibrosis of anterior wall, diffuse active syphilitic myocarditis, aortic syphilis; brown induration of lungs with acute edema; fibrosis, atrophy and chronic passive congestion of all organs, orchitis fibrosa syphilitica, syphilitic scar on penis, varicocele.

CASE IV.—Autopsy T—IV, 1915. Mr. F., aged twenty-five, student. Father died at thirty-nine years of age of cardiac syphilis. Patient had two brothers with evidences of congenital syphilis who died in infancy, and another brother of adolescent age who died with cardiac symptoms. As a child he himself had also clinical manifestations of the same disease, but since adolescence had had fairly good health,

and was just finishing a course in engineering. In July, 1915, he went into active field work, while suffering from a severe attack of gonorrhea, and after a few days of strenuous labor in hot weather he suddenly developed marked signs of cardiac insufficiency, cyanosis, dyspnea and pulmonary edema. The latter was so marked that a constant flow of blood-tinged fluid came from his respiratory tract, and he was thought to have croupous pneumonia. He was brought at once to the University Hospital. Physical examination showed marked signs of cardiac dilatation and inadequacy. Death took place three days after the beginning of his symptoms. The autopsy (at coroner's request) showed an enormously enlarged and dilated heart, the enlargement involving particularly the left ventricle. The anterior wall of the latter showed an aneurysmal dilatation extending to the apex. When the heart was opened this dilatation was found to be filled with a recent red thrombus

Fig. 4.—Section of left ventricle wall from Case IV. Area of recent syphilitic myocarditis.

slightly attached to the endocardium over the thinned wall of the aneurysmal dilatation. This thin wall consisted of pale yellow heart muscle showing no fibrosis and no hemorrhage. Similar pale patches and streaks occurred in the myocardium of the septum and other portions of the left ventricular wall. There were no endocardial lesions except cloudiness and discoloration of the endocardium at the site of the thrombus. Bacteriological examination, especial search for gonococci being made, was negative. Fresh embolic anemic infarcts were present in the spleen and liver, but no organisms were found in the emboli. The lungs showed no pneumonic areas, but extreme congestion and edema with multiple fresh, hemorrhagic infarcts. Microscopical study showed an acute syphilitic myocarditis of the entire heart wall, most marked in the anterior portion of the left ventricle and in the septum. The lesions consisted of lymphocyte, plasma cell and polymorphonuclear infiltrations, with older areas of fibroblastic proliferation and scattered patches of fibrosis and atrophic muscle fibers (See Figs. 4 and 5). Spirochetes were demon-

strated in the acute infiltrations in great numbers; no other bacteria were found, although great numbers of sections were stained for such. Small active syphilitic lesions were found also in the aortic wall. The complete *pathological diagnosis* was: Cardiac thrombosis, aneurysmal dilatation of left anterior ventricular wall above apex. Chronic syphilitic (congenital) myocarditis with acute exacerbation. Cardiac insufficiency. Multiple recent anemic infarcts in spleen and kidneys. Multiple recent hemorrhagic infarcts of lungs. Extreme pulmonary congestion and edema. General passive congestion. Acute gonorrheal urethritis and prostatitis.

CASE V.—Autopsy 37-X, 1919 (Coroner's case). A. V., Greek laborer, aged about forty-five (?), working on a construction gang, had several attacks of dizziness and shortness of breath for two to three days before his death, compelling him to

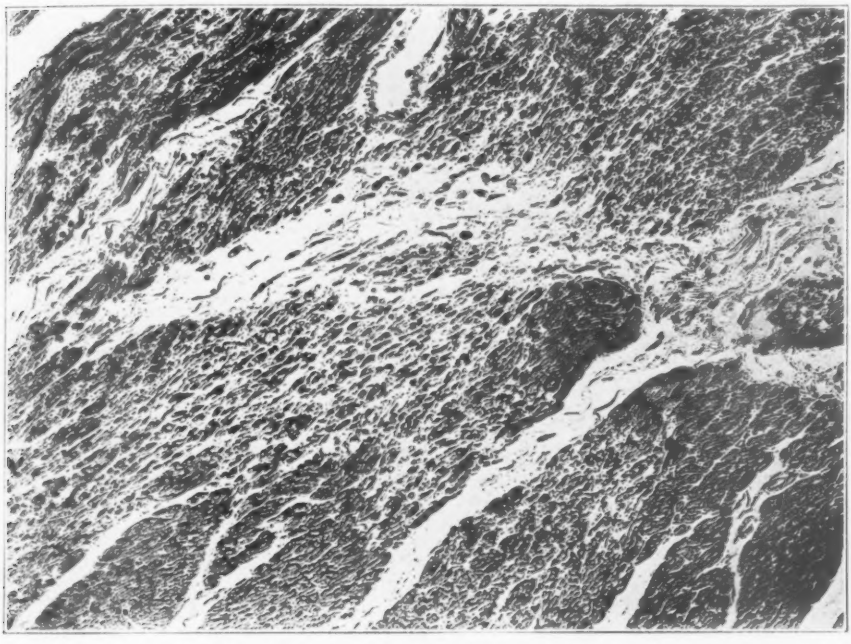

Fig. 5.—Section of wall of left ventricle from Case IV showing older healed area of syphilitic myocarditis. Atrophic muscle with increase of stroma.

sit down for rest. On the day of death he complained of palpitation and cardiac distress, staggered to the sidewalk and sat down on the curb. An ambulance was called, and he was taken to the University Hospital, dying on the way. Autopsy showed a moderately enlarged heart, the right side showing the greater dilatation; no valvular lesions were present. Sections of the myocardium showed small grayish patches throughout the muscle. Arch of the aorta presented a moderate degree of sclerosis. Microscopical examination showed a marked diffuse syphilitic myocarditis and fibrosis, an older process with acute exacerbation, as shown by recent infiltrations of lymphocytes, plasma cells and polymorphonuclears. Spirochetes were demonstrated in these areas. The complete *pathological study* showed the following: Old syphilis; fibroid myocarditis with acute exacerbation; syphilitic mesaortitis, pancreatitis, adrenalitis and orchitis. Cerebral syphilis; syphilitic lesions in hypophysis; syphilitic glossitis, acute passive congestion of all organs, pulmonary edema; lipoidosis of adrenals; slight fatty liver.

CASE VI.--Autopsy 194-AB, 1924 (Coroner's case). Mr. W. G. P., aged 44, traveling salesman, married, no children. Previous history of good health, except for occasional burning sensation in throat. Came home from a trip in June, 1924, complaining of fatigue, from which he sought relief by lying down. At four-thirty in the afternoon went for an automobile drive, appearing to be somewhat abstracted and less talkative than usual. Returning he ate his usual dinner, after which he and his wife went out for a short walk. During this walk he made several gasping sounds alarming her so that she asked if he was having difficulty in breathing. He replied that he had a peculiar burning sensation in his throat extending to the middle of his chest and radiating into his back and down his right arm. During the walk he had several other gasping attacks, so that they decided to visit a physician on the way home. In the latter's office he appeared to feel very much better, and

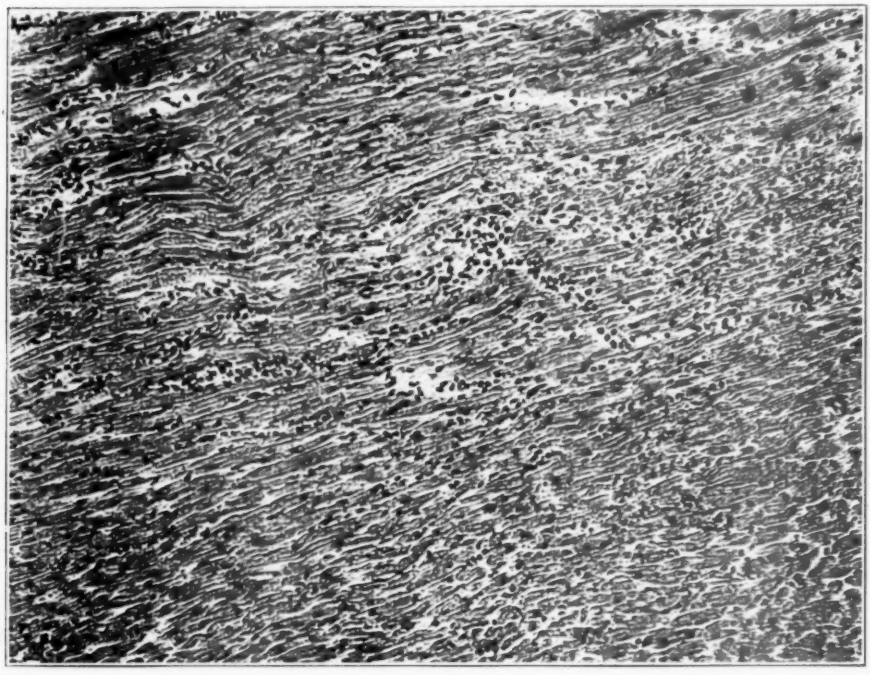

Fig. 6.—Low power view of acute syphilitic myocarditis from Case VI. Slight diffuse infiltration, largely polymorphonuclear.

laughed and joked about the situation. The physician found his throat to be very congested, and gave him some "tonsillitis tablets" and told him to gargle with warm milk. On his return he used the gargle and took tablets as directed. At 10:15 P. M., he said he felt perfectly well, and fifteen minutes later was sleeping soundly in bed. At 2:00 A. M. his wife was awakened by his unusually loud snoring. While attempting to arouse him he suddenly stopped snoring and breathing for a brief period, then gave a loud groaning gasp and his stertorous breathing was resumed. His wife becoming alarmed, and seeing that he was getting blue in the face tried again to rouse him, but he became more and more cyanotic and ceased breathing in a short time. The autopsy, at coroner's request, showed a slightly enlarged heart; there were numerous minute petechial hemorrhages beneath the pleurae and epicardium; both right and left ventricular walls were hypertrophic, on section brownish-red in color, and no areas of fibrosis or infarction were visible to the naked eye. The valves were negative. Coronaries negative save for a slight degree of

sclerosis. Lungs markedly congested and edematous. The aorta showed a marked degree of syphilitic mesaortitis. The microscopical examination of the heart showed a diffuse myocarditis; throughout the entire heart wall, but especially marked in the septum and left anterior ventricular wall, the myocardium showed infiltrations of lymphocytes, plasma cells and groups of polymorphonuclears between the muscle fibers. These infiltrations appeared as cord-like or columnar rows of cells separating the muscle fibers, but nowhere large enough to be visible to the naked eye (Figs. 6 and 7). No infarctions or areas of fibrosis found in the heart wall. The inflammatory infiltrations increased toward the aortic valves and aorta, and the aortic wall showed an advanced and very active syphilitic mesaortitis. Spirochetes were found in great numbers in aorta and heart wall, (See Fig. 21). The complete *pathological diagnosis* was as follows: Cardiac death. Cardiac hypertrophy and dilatation. (Angina pectoris ?). Advanced syphilitic aortitis with acute exacerbation. Acute

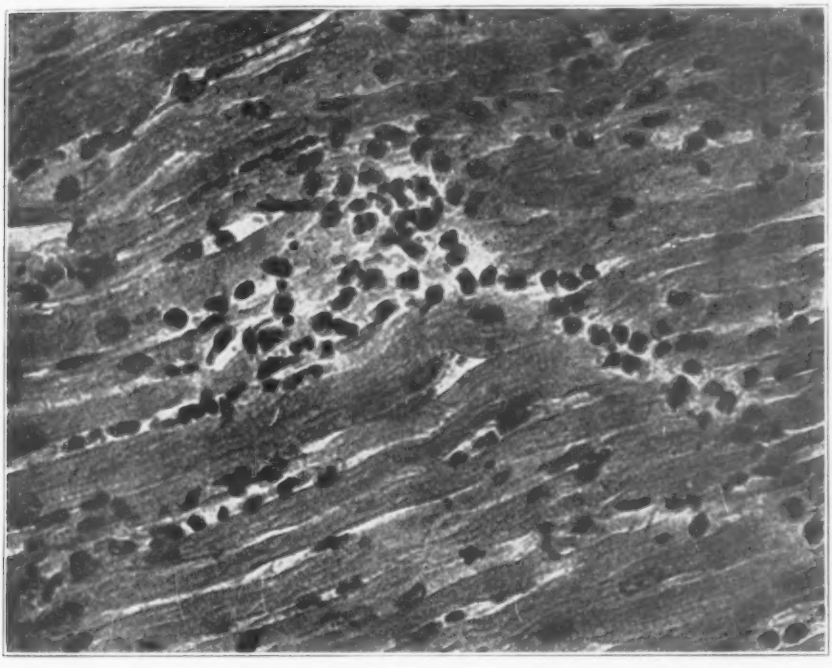

Fig. 7.—High power view of preceding figure showing the character of the acute syphilitic reaction:—lymphocytes, plasma cells, mononuclears and polymorphonuclears. Heart muscle shows but slight change.

syphilitic myocarditis. Pulmonary stasis, hemorrhage and edema. Edema of upper respiratory tract. Chronic syphilitic leptomeningitis. Atherosclerosis of cerebral arteries. Acute passive congestion of all organs. Colloid adenomatous goiter. Persistent thymus. Hypoplasia of adrenals with lipoidosis. Old obliterative appendicitis. Chronic perihepatitis. Old pleural adhesions. Old calcareous tubercles in lungs, bronchial nodes, spleen and liver. Meckel's diverticulum.

CASE VII.—Autopsy 35-AC, 1924, D. H., aged 57, American, business man. Had syphilis at the age of nineteen, was thoroughly treated according to the methods of that time, but during his twenties developed optic atrophy, which was arrested by a further course of treatment, but left him with much diminished eyesight. From this time on he had very fair health, although not very strong in build. Married, without children, wife never pregnant. Managed a large business successfully, and

active in civic work. Later in life had several negative Wassermann reactions. Had complained for several days of fatigue and slight shortness of breath. On the day of his death had precordial distress and pain extending down right arm, and did not go to his business. He felt somewhat better later in the day, and went into the bathroom where he was found dead. Autopsy (request of family and coroner) showed moderate hypertrophy and dilatation, particularly marked in the left ventricle. No areas of fibrosis seen by the naked eye, but small yellowish patches suggesting fatty change occurred throughout the myocardium, and were most numerous and more marked in the neighborhood of the mitral and aortic valves. No endocardial lesions except a slightly roughened area near the aortic ring. The coronaries showed marked thickening, without obliteration, in their proximal portions, while the distal branches appeared normal. Patches of typical syphilitic aortitis occurred throughout the

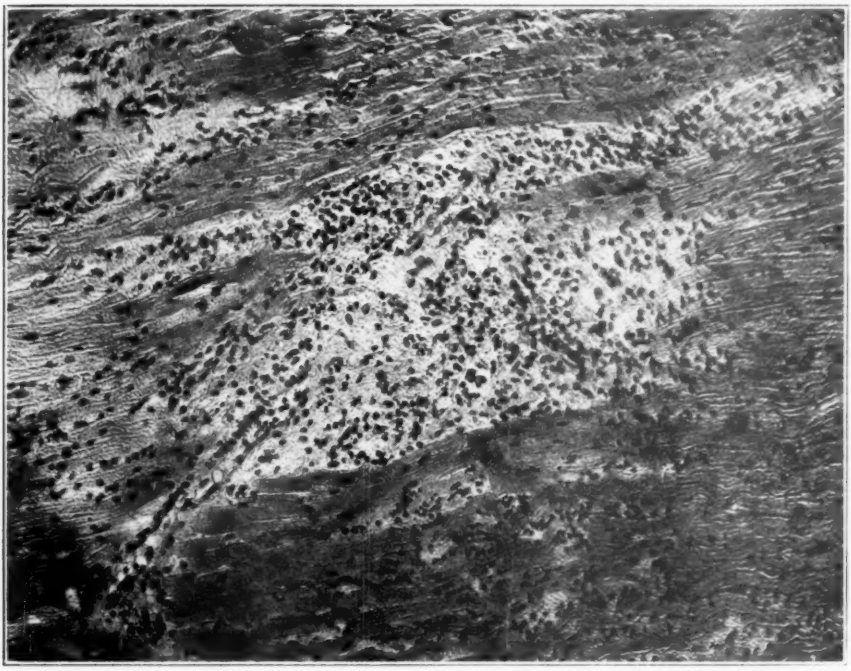

Fig. 8.—Area of marked acute syphilitic myocarditis from left ventricle wall of Case VII. Infiltration consists of lymphocytes, plasma cells and mononuclears with foci of numerous polymorphonuclears.

aortic arch. The microscopical examination showed a marked atrophy of the heart muscle with localized marked fatty degenerative infiltration, particularly near the endocardium. The myocardium of both ventricles but especially that of the left showed a marked diffuse interstitial myocarditis of syphilitic type, the infiltrations consisting of lymphocytes and mononuclear cells with areas of polymorphonuclears (See Figs. 8 and 9). In the areas of marked interstitial infiltration there was also a marked interstitial edema. In these areas the heart muscles was atrophic and showed marked fatty change. No definite areas of infarcts were found; and only small areas of older fibrosis. Both epicardium and endocardium showed areas of plasma cell infiltration and fibroblastic proliferation. The larger coronary branches showed the histological picture of an active syphilitic arteritis. The aorta presented localized areas of advanced and more active syphilitic mesaortitis. Spirochetes were found in numbers in the interstitial infiltrations of the myocardium (See Fig. 20).

The complete study gave a *pathological diagnosis*, as follows:—Syphilitic aortitis and coronary arteritis. Active syphilitic myocarditis. Atrophy, fatty infiltration and fatty degenerative infiltration of heart muscle. Dilatation of left ventricle. Right side cardiac dilatation with relative tricuspid insufficiency. Cardiac death. (Angina pectoris?) General arteriosclerosis. Early arteriosclerotic kidney with small healed infarcts. Early orchitis fibrosa syphilitica. Slight chronic prostatitis with glandular hyperplasia and cystic dilatation. Phleboliths in prostatic plexus. Cholelithiasis. Fatty atrophy of pancreas. Persistent thymus. Hypoplasia of adrenals. Focal chronic leptomeningitis (syphilitic). Optic atrophy. Old iritis. Scar of lower lip. Diverticulum of bladder.

CASE VIII.—Autopsy 142-AC. (Coroner's case). F. G., aged twenty-nine, American motorman, was admitted to the University Hospital March 23, 1925, complain-

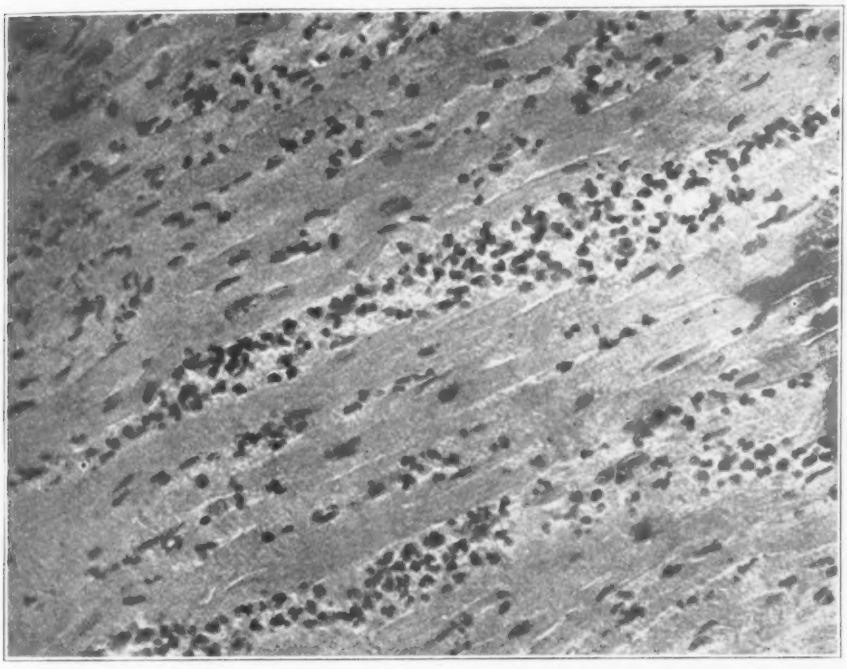

Fig. 9.—Higher power view of section from left ventricle wall of Case VII showing areas in which the infiltration consists largely of polymorphonuclear cells. Spirochetes were found in sections adjacent to this one.

ing of shortness of breath, swelling of the ankles and weakness. Ten months before admission the patient noticed that he was becoming short of breath and had cardiac palpitation on exertion. He continued at his work. About four months before admission his ankles began to swell and were more swollen in the evening. Two months before admission he gave up his work because of increasing palpitation, dyspnea and weakness. His physician prescribed tincture of digitalis. He felt stronger and returned to work for nine days in January. He soon had to stop, however, and the weakness and edema became progressively more marked. Ten days preceding admission he was forced to sleep in a chair because of shortness of breath. He also had dull pain in the lower chest and difficulty in walking because of weakness. Three days before admission he coughed up one-half ounce of bright red blood. None before or since. The patient had had mumps but no other illnesses. He denied venereal disease. He had had no gastrointestinal symp-

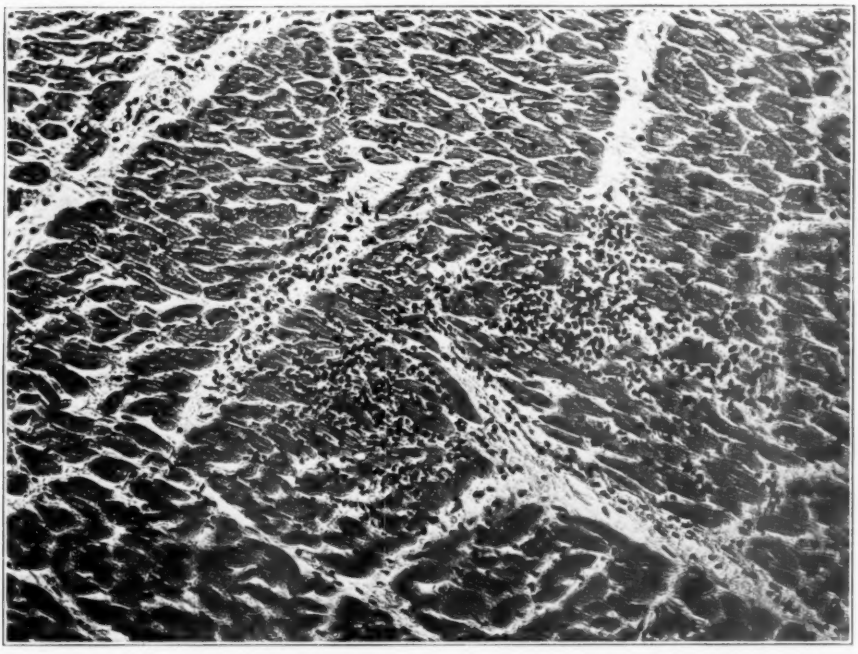

Fig. 10.—Lower power view of small localized recent syphilitic infiltrations in ventricle wall of Case VIII.

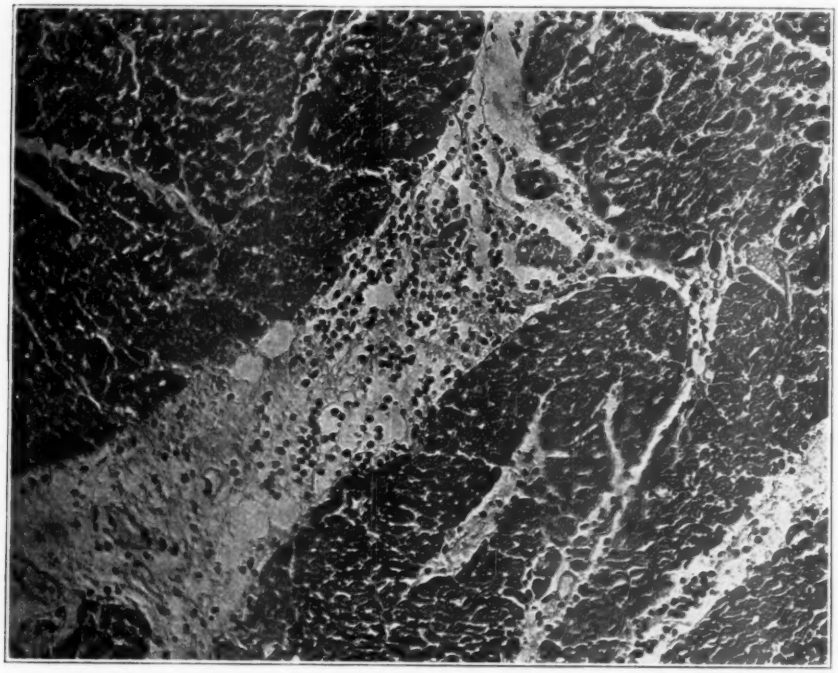

Fig. 11.—Lower power view of acute syphilitic reaction between cardiac muscle bundles. The connective tissue is very edematous and diffusely infiltrated with cells, the character of which is better shown in Fig. 12, Case VIII.

toms and had lost no weight. Father died of inflammatory rheumatism at forty-five. The mother died of "ascending paralysis" at forty-eight. The patient had one brother and two sisters living and well. None dead. There was no family history of cancer, tuberculosis, or insanity. Patient was orthopneic and distinctly pale. The skull, scalp and hair were negative. The pupils reacted sluggishly to light and the left was slightly larger than the right. The lips and mouth were negative. Many of the teeth were carious. The tonsils were small and not reddened. The thyroid was not palpable and no lymph glands could be felt in the neck. The thorax was symmetrical. Respirations about 30 per minute. The heart was greatly enlarged, the apex beat being felt about 14 cm. from the midsternal line in the fifth intercostal space. The precordium heaved with each systole. A long, loud, blow-

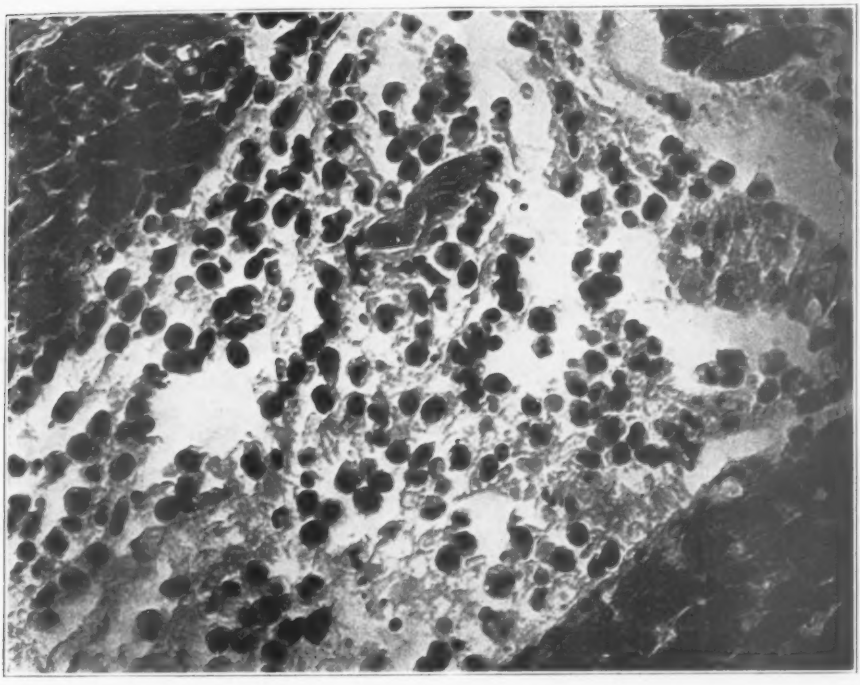

Fig. 12.—Higher power view of preceding figure showing the types of cells of the most acute form of the syphilitic reaction. Spirochetes were most numerous in such areas.

ing systolic murmur was heard at the apex and the second sound was reduplicated. The retromanubrial dullness was increased. The blood pressure was 100/88. The lungs were negative except for coarse râles at the bases. The liver could be felt 3 finger-breadths below the costal margin. The spleen was not palpable. The lymph glands of the axilla, epitrochlear region and groin were not palpable. There was marked edema of the lower extremities extending up to the knees. The blood and urine were not examined. The Wassermann was later reported negative. The patient was regarded as an example of pronounced cardiac failure. He was placed in bed and given a cardiac diet with limited fluids. Morphine sulphate, grains ¼ by hypodermic injection every four hours, was prescribed. He received the first dose at 5 o'clock, March 23, and a second dose at 10:45. He was nauseated and vomited, then dropped into a deep sleep. At about 2:30 on the morning of March 24, it was noticed that the respirations were very slow but the patient awoke and

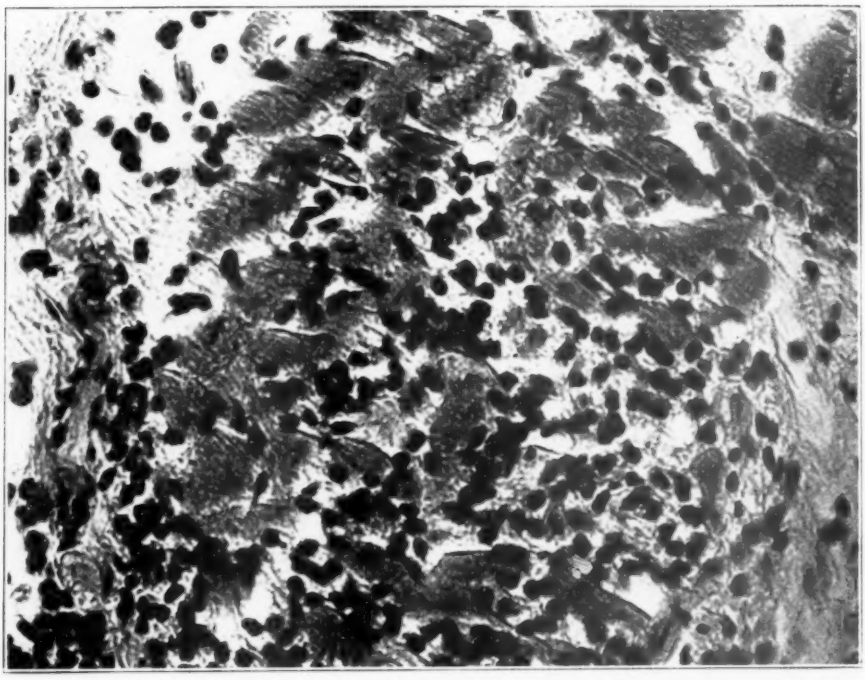

Fig. 13.—Acute syphilitic myocarditis from Case VIII. These areas are pale-yellow, or grayish-yellow, or gray to the naked eye, and in the gross may be easily mistaken for anemic infarcts. The muscle is not necrotic, but is usually fairly well preserved, and there is no hemorrhagic or congested zone about such infiltrations.

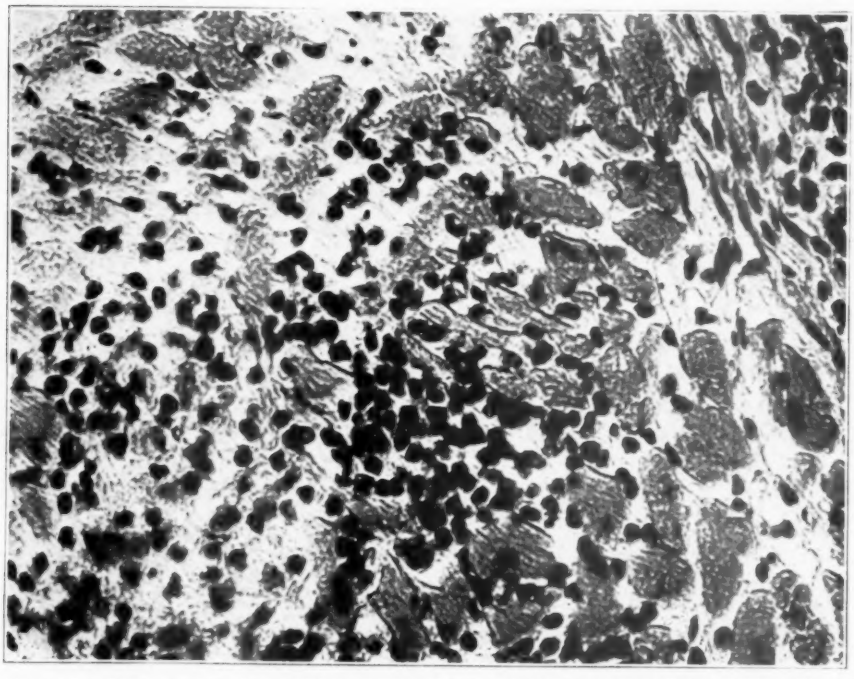

Fig. 14.—Older area of syphilitic infiltration in heart wall of Case VIII. Heart muscle is more atrophic, and fibroblastic proliferation (left) is more marked.

talked to the nurse. He died suddenly at 3:15 A.M. During the patient's stay in the hospital his temperature was subnormal. Since cardiac failure without valvular lesions is uncommon in patients below thirty, except as a result of the acute myocarditis of rheumatic fever or diphtheria, the diagnosis was cardiac failure of myocardial origin, acute rheumatic heart disease (?). (Dr. F. N. Wilson.)

The autopsy showed a greatly dilated heart, apex in sixth intercostal space slightly posterior to the anterior axillary line. The right border of the heart was 5 cm. to the right of the midline. The apex was formed equally of right and left ventricles. The left ventricle was about twice as large as the right. Epicardial surface clouded, and the subepicardial fat scanty and very pale in color. There were a few subepicardial petechial hemorrhages. The left ventricle was much dilated and globular in shape, the papillary muscles being much flattened. The ven-

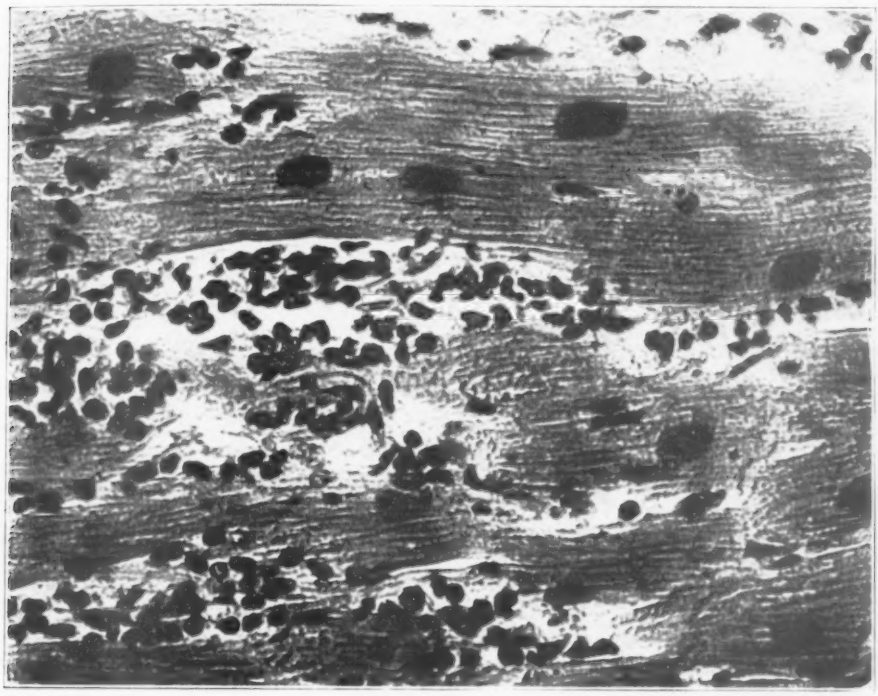

Fig. 15.—High power view of acute syphilitic reaction in myocardium of Case VIII. The well-preserved heart muscle fibers differentiate such areas from the toxic myocarditis of diphtheria, typhoid, etc. The infiltration in this area is largely polymorphonuclear.

tricle wall measured 12 mm. in thickness; wherever sectioned it showed patchy and streaked grayish-white areas throughout the myocardium. These areas were somewhat depressed below the cut surface of the surrounding musculature, and were interpreted in the gross as areas of fibrosis. There was no hemorrhagic or congested zone about the pale areas. The valvular orifices were all dilated; the valve flaps negative. The coronary vessels were all negative. The aorta showed nothing to the naked eye but a slight lipoidosis of the intima. The gross pathological diagnosis was that of active luetic myocarditis. The microscopical examination showed that the pale areas in the myocardium consisted wholly of inflammatory infiltrations and fibroblastic proliferations, many of the largest ones distinctly gummatous in type, consisting of an atypical vascular granulation tissue infiltrated with lymphocytes, plasma cells and some polynuclears. Some giant cells were found in these young

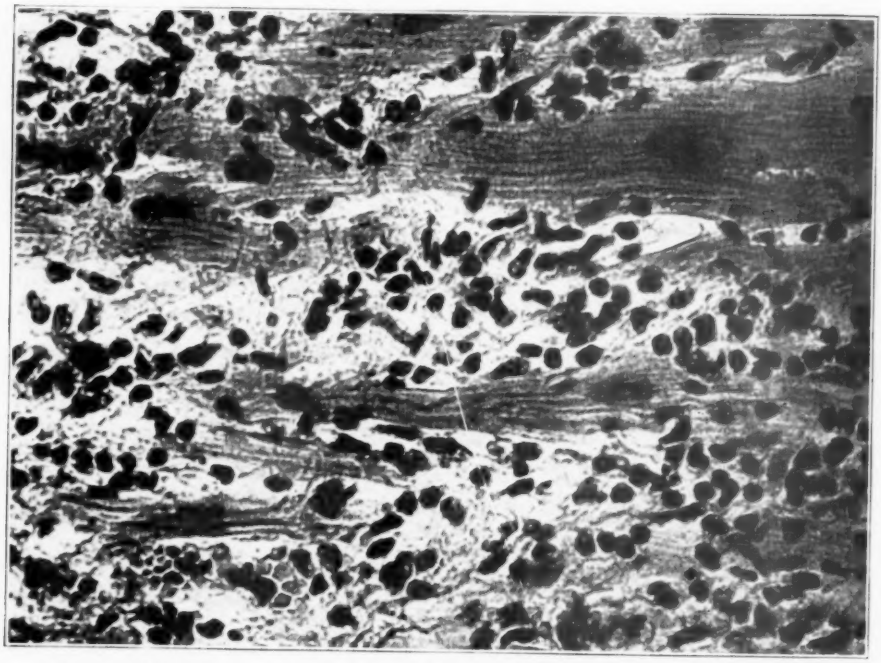

Fig. 16.—More advanced area of syphilitic myocarditis from ventricle wall of Case VIII. Infiltration shows more lymphocytes and plasma cells and fewer polymorphonuclears. Heart muscle is showing atrophy in the denser infiltration. Fibroblastic proliferation with characteristic interstitial edema.

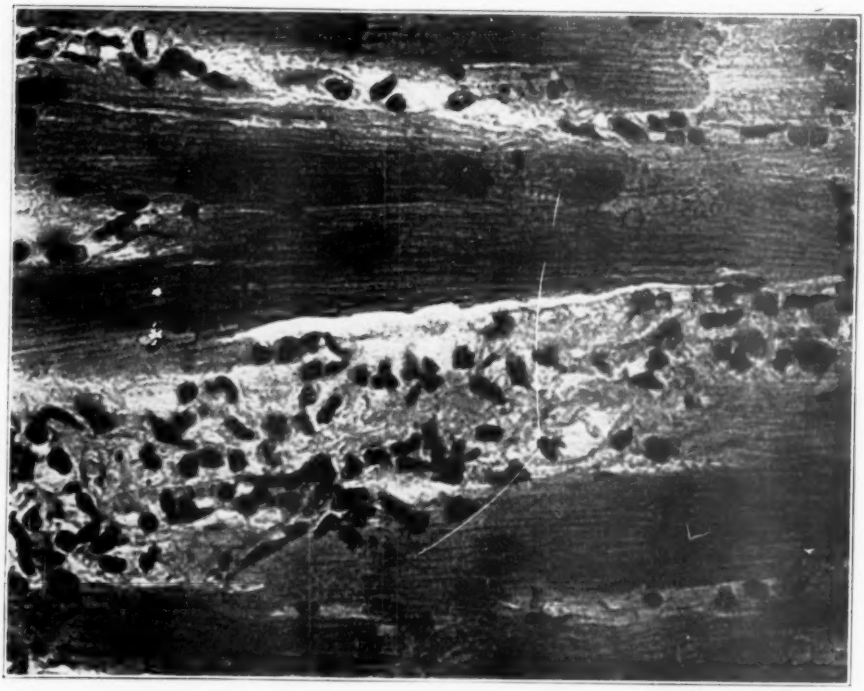

Fig. 17.—Higher power to show the character of the interstitial edema and infiltration. Such areas resemble the lesions in congenital syphilis of the myocardium of the newborn.

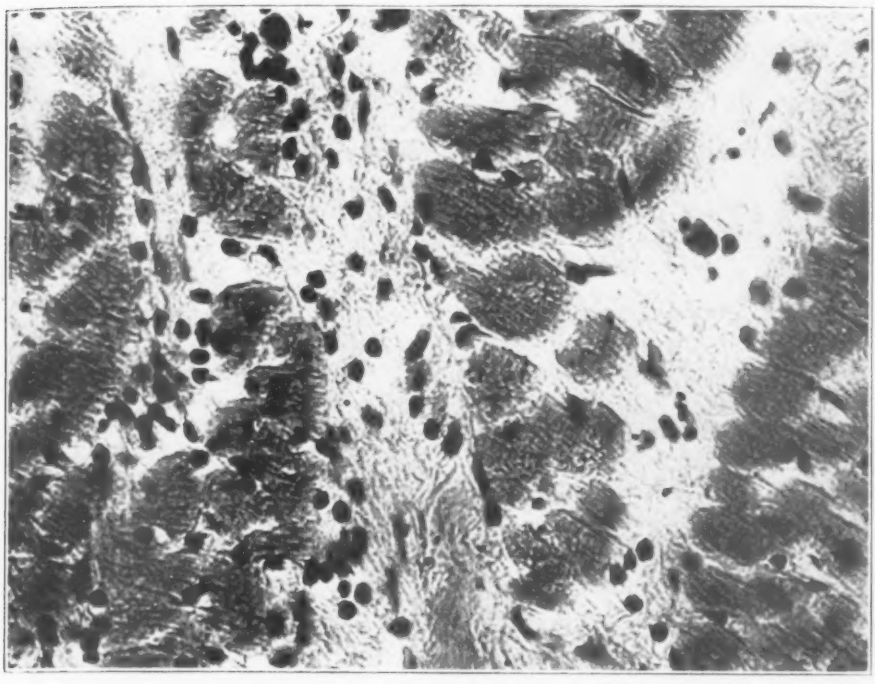

Fig. 18.—Older, more fibroid area of syphilitic myocarditis from Case VIII.

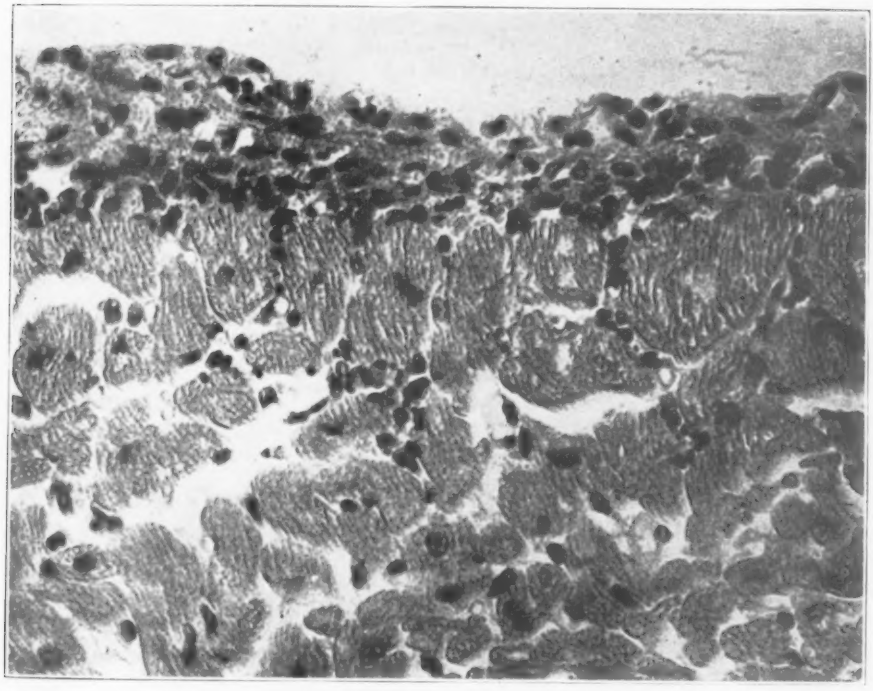

Fig. 19.—Characteristic subendothelial infiltration and proliferation of acute syphilitic myocarditis from Case VIII.

gummatous lesions. There was no caseation. Older, more fibroid areas were present near the endocardium. Throughout the heart wall all stages of reaction from an early interstitial edema and polymorphonuclear infiltration, lymphocyte and plasma cell infiltration, fibroblastic and angioblastic proliferation, definite gummatous granulomas to completely healed and fibroid areas were present. In some areas the lesions extended from endocardium to epicardium. The more acute and active areas predominated. Spirochetes were demonstrated in these areas. The coronary vessels themselves showed no change; but many of them were surrounded by lymphocyte and plasma cell infiltrations. The endocardial surface showed microscopically a cell proliferation and infiltration beneath the endothelium. No evidences of a thrombo-endocarditis were present. No infarcts found. The epicardium showed a slight lymphocyte infiltration just beneath the surface, with a thin line of fibrin on the surface. Sections of the aortic valve showed small active lesions of the media and adventitia. The complete *pathological diagnosis* was as follows: Active syphilis. Diffuse gummatous myocarditis of left ventricle and septum with acute cardiac dilatation. Cardiac insufficiency. Brown induration of lung with acute pulmonary stasis and edema. Hydrothorax, hydropericardium, ascites. Nutmeg liver. Small gumma in liver. Syphilitic lesions in lungs, aorta, meninges, tonsils, lymph nodes and testes. Atrophic catarrhal gastroenteritis. Persistent thymus. (See Figs. 10 to 19 inclusive.)

DISCUSSION OF THE CASES

Clinical Features.—The most striking clinical feature of this group of cases is the very abrupt onset of marked symptoms of cardiac insufficiency in individuals apparently in good health and going about their usual occupations. In Case VIII only, had symptoms of cardiac incompetency been noted for some months, and the patient continued at work until two months before his death. The greater degree of involvement and the more severe character of the older process in this case explains the longer duration of the symptoms. In Case I the symptoms were of about twenty-four hours' duration; in Case II a few hours only, in Case III a few days, in Case IV three days, Case V two to three days, Case VI a few hours, Case VII several days, while in Case VIII the severe symptoms manifested themselves in the last ten days of his life and he was practically moribund when admitted to the hospital. In all but Case VIII the death was so sudden and unexpected that the cases became coroner's cases, and in this instance also the character of the symptoms and the sudden death within twenty-four hours after admission were so unusual in a young man that a coroner's request for autopsy was considered desirable.

Shortness of breath and cyanosis were the most common symptoms in all of the cases. Vague precordial or chest "distress," or definite pain radiating toward the back and down the right arm, poorly defined anginal symptoms, palpitation, dizziness, marked fatigue or exhaustion, burning sensation in throat, and epigastric distress constituted the other symptoms. In only four of the cases was the patient seen by a physician before his death; in Case III the patient was admitted to the hospital with severe symptoms of acute cardiac insuf-

ficiency and died within twenty-four hours. No clinical examination was made. In Case IV the severity of the pulmonary edema led to a clinical diagnosis of pneumonia; in Case VI the physician made no cardiac examination and apparently suspected no cardiac condition; in Case VIII alone was the patient recognized as an example of pronounced heart failure, and his physical signs and symptoms noted just before his death. The patients were all males. Their respective ages were fifty-three, forty-two, fifty-five, twenty-five, forty-five (?), forty-four, fifty-seven, and twenty-nine. It will be noted that all of these ages are too early for marked senile vascular changes, or for cardiac

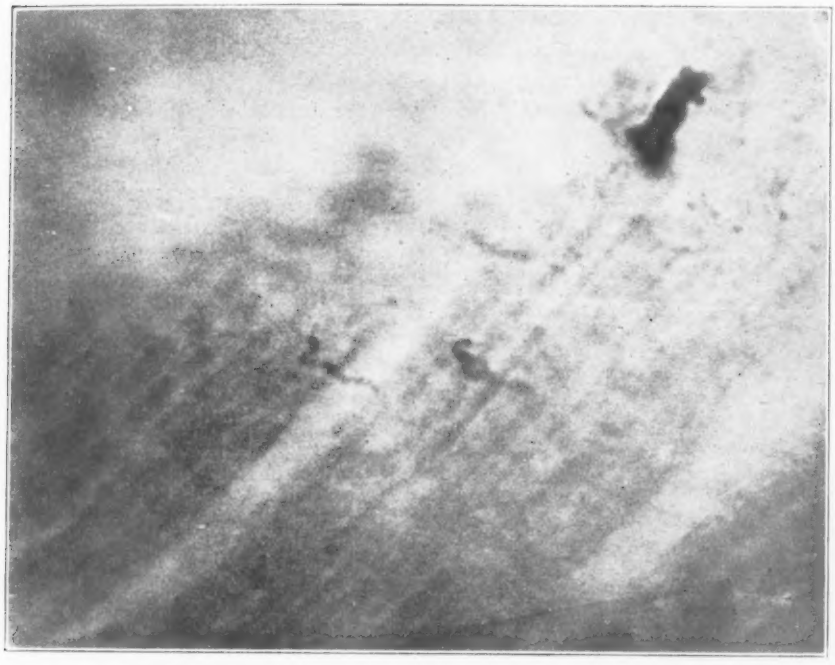

Fig. 20.—Two spirochetes lying over muscle fibers, from area of infiltration in Case VII. Spirochetes are but partly in focus, the organisms not lying in parallel planes.

lesions due to age alone. This clinical feature in itself should indicate the existence of cardiac disease of an infective or toxic nature.

As to the clinical facts indicating the etiological factor in these cases syphilis was indicated by the family history in Case I, was positively known to have been present in Cases II, IV (congenital) and VII. Venereal infection was denied in Cases III and VIII. No clinical history was obtainable in Case V, and in Case VI there was also no opportunity to obtain any clinical history as to the occurrence of syphilitic infection. The oldest patient (fifty-seven) had a known history of a well-treated syphilis contracted early in life.

As to the clinical possibility of other infections, rheumatism, diph-

theria, typhoid fever, etc., playing an etiological rôle, the clinical history as obtained was negative in each case. The clinical suspicion of rheumatic fever as the causal agent of the cardiac failure in Case VIII was based wholly upon the age of the patient, the absence of valvular lesions and of other positive evidence as to the existence of syphilis or other infection. The patient, himself, gave no history of rheumatic symptoms.

Summing up the clinical evidence, we have eight cases in young and middle-aged males of very sudden or rapidly developing symptoms of cardiac incompetency terminating quickly in death, without valvular

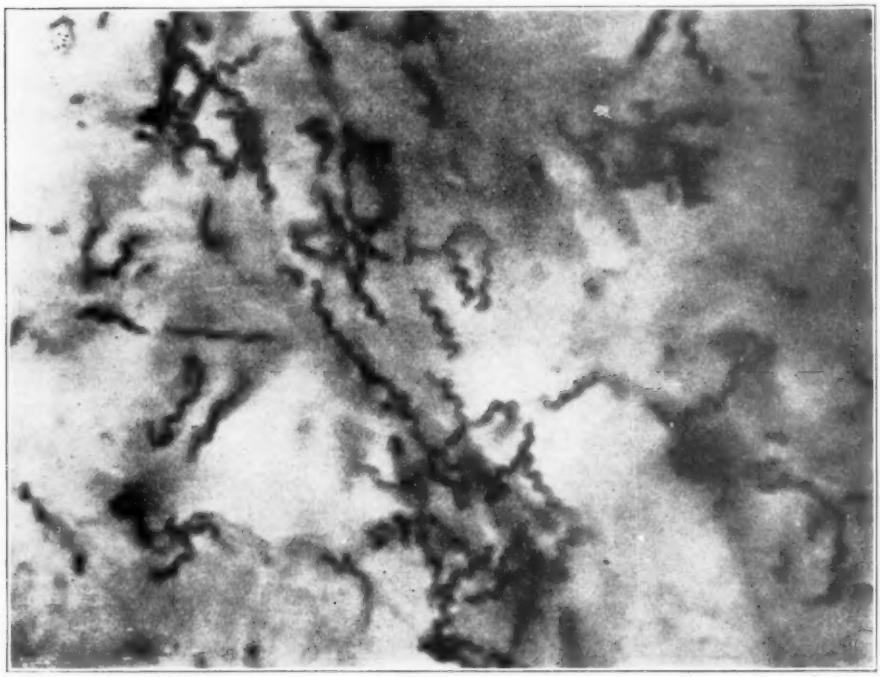

Fig. 21.—Area containing numerous spirochetes, from wall of left ventricle, near the aortic ring. Many organisms in same focal plane. Case VIII.

lesions, and without clinical history of rheumatism, streptococcus infections, diphtheria or typhoid, but with a known clinical history of syphilitic infection in four cases (50 per cent), denied in two cases (25 per cent), and no clinical history obtainable as to syphilis in two cases (25 per cent).

Overexertion and heat appear as exciting factors in the final breakdown.

Pathology.—The gross pathological features were: cardiac dilatation, particularly of the left ventricle but in some cases marked also on the right; in three cases there was a well-defined aneurysmal bulging of the anterior wall of the left ventricle above the apex; in one

case it was as large as a small orange, and could well be classed as a cardiac aneurysm. Cardiac thrombosis was associated with these localized dilatations of the left ventricle in two of the cases. The myocardium presents varying degrees of hypertrophy, atrophy and parenchymatous degeneration, particularly fatty degenerative infiltration.

The most striking gross features in the great majority of the cases were the patchy and streaked areas of pale yellowish, grayish-yellow or gray color, without hemorrhage or congestion, scattered throughout the myocardium, particularly that of the left ventricle and septum, and usually more marked in the left anterior wall extending to the apex. The patches occur most frequently in the middle layer of the myocardium, but frequently near the endocardium. In the extreme cases they may reach from endo- to pericardium. They are more streaked and irregular in outline than are anemic infarcts. These patches, when most marked, may easily be taken for anemic infarcts, and probably are in the usual pathological routine, but the entire absence of evidence of hemorrhage, their semitranslucent, slightly depressed surface should at once put the pathologist on his guard and lead him to consider myocardial infiltration rather than infarction. In Case VII the patches were mistaken for localized fatty change. It also must be emphasized that extensive infiltrations between the muscle fibers may occur without any marked gross changes, and may be revealed only on microscopical examination as in Case VI, in which the prosector failed to note any color changes in the myocardium. No valvular lesions or evidences of thromboendocarditis were found in any of the cases; and localized pericardial lesions in only three of them.

The general pathological picture of cardiac incompetency is present. Chronic passive congestion of the lungs (brown induration) was found in varying degrees in all, indicating a longer duration of cardiac weakness (left ventricle) than the clinical history would indicate. Upon this is superimposed the picture of an acute exacerbation of the congestion with extreme pulmonary edema, and in two cases slight pulmonary hemorrhage from diapedesis. Pulmonary thrombosis and acute hemorrhagic infarction may be added to this. Throughout the body the usual picture of cardiac insufficiency is found in the generalized passive congestion, edema, collection of fluid in the body cavities, petechial hemorrhages, and occasional thromboses and infarctions.

Pathological evidences of latent syphilis occur particularly in the aorta, which usually shows an exacerbation also of the syphilitic process. This was most marked in Case VI, the microscopic lesions in the aorta being even more marked than those in the myocardium. The aorta may show very little gross changes in such cases, and the microscopical examination is essential to the diagnosis. Lesions of latent

syphilis, more or less active, are found especially in the leptomeninges, liver, pancreas, adrenals and testes. Our Case VIII showed a picture of a generalized active late syphilis in a stage of very active exacerbation (critical stage) of the disease. It is very probable that this young man's syphilis was only several years old, and had not been treated at all or only very inadequately. The diagnosis of these scattered syphilitic lesions is essentially microscopical.

Microscopical Pathology.—The microscopical features of the cardiac lesions were areas of old fibrosis (completely healed myocarditis); subacute infiltrations of lymphocytes and plasma cells between the muscle fibers, with angioblastic and fibroblastic proliferation and interstitial edema; more acute areas of interstitial edema with infiltrations of lymphocytes, plasma cells, monocytes and a predominance of polymorphonuclears. Spirochetes were found, particularly in these more acute areas. All stages of syphilitic myocarditis are represented in these lesions. Miliary gummas with giant cells were occasionally found (particularly in Case VIII), but no caseating ones occurred in any case. The coronary changes were relatively slight except in Case III in which the anterior left descending branch showed extensive syphilitic arteritis. No Aschoff nodes were found in any case.

The microscopical lesions in the aortas of these cases also represented various stages of syphilitic mesaortitis consisting of similar infiltrations along the vasa vasorum, most marked in the adventitia and outer portion of media. The aortic lesions were most marked in Case VI, and spirochetes were especially numerous in the aortic lesions of that case.

The syphilitic lesions in other organs consisted of fibrous thickening, lymphocyte and plasma cell infiltrations, and occasionally miliary gummas, as in Case VIII. The majority of these lesions were microscopical only; few could be recognized by the naked eye. They occurred especially in the leptomeninges, liver, pancreas, adrenals and testes. The parenchymatous changes throughout the body consisted essentially of atrophy, with slight fatty degenerative infiltration and cloudy swelling.

CONCLUSION

These eight cases show that sudden death may occur in latent syphilis as the result of an acute exacerbation of previously mild, latent processes in the heart and aorta. The pathological character of the active lesions differs from that of the chronic lesions in the more marked edema and the greater polymorphonuclear cell content of the infiltrations. In this respect these acute lesions resemble the perivascular and vascular infiltrations of active syphilis of the umbilical cord in which the cells are predominantly polymorphonuclears and the number of spirochetes enormous. They correspond also to the "critical reaction" described by Wade Brown and Louise Pearce in experi-

mental animal syphilis in which there is a diffuse edema and polymorphonuclear infiltration in the rapidly developing syphilitic lesions followed by a rapid resolution. Similar lesions occur in the earliest stages of the syphilitic process, and in lesions of malignant type before ulceration occurs. Very acute and active syphilis is characterized by more diffuse lesions, more marked edema and a greater number of polymorphonuclear cells in the infiltration. The typical picture of perivascular lymphocyte and plasma cell infiltration and eventually fibrosis will, however, always be associated with these when the active process is an exacerbation of an older latent syphilis. According to Brown the polymorphonuclear infiltration of the critical reaction is just as typical for syphilis as is the focal round cell infiltration for the chronic type of syphilitic process. This fact may not be recognized by the pathologist who carries in his mind the mononuclear type of infiltration as the characteristic diagnostic picture of syphilis, and he may, therefore, fail to recognize the polymorphonuclear malignant type of syphilis. At any rate, the demonstration of the spirochete in the latter type of lesion is the only decisive diagnostic point, and must be accomplished to fix the diagnosis, and unless this is done such cases will escape proper interpretation. Unfortunately for the recognition of these cases, in how many pathological laboratories are routine examinations for spirochetes made?

The factors leading to such an increase of virulency in chronic latent cases are still unknown, beyond the vague conception of lower resistance due to overstrain, fatigue, other infections and intoxications, endocrinal changes, other environmental influences, etc.

Much is being said at the present time as to the great frequency and apparent increase of cardiac disease, but the important if not predominant rôle played by syphilis in the production of myocardial incompetency is not recognized by the major part of the profession, internists as well as pathologists. While some practitioners of large experience are fully aware of the importance of syphilitic myocardial changes, others fail to recognize it; and the same is true of pathologists. In a recent article, Clawson (Amer. Jour. of Med. Sciences, November, 1924, page 654) says that "luetic myocarditis is rare." This is so contradictory to my own experience that I can only explain it on the ground of a failure of recognition and proper interpretation of myocardial lesions and a failure to demonstrate the association of spirochetes with such lesions. In my own experience in Michigan, syphilitic cardiovascular lesions are very common, and are more frequently associated with cardiac incompetency than is coronary disease or streptococcus, rheumatic, diphtheria or typhoid myocarditis. The systematic pathological examinations (microscopical) of hearts of paretics, tabetics and other old syphilitics will show characteristic myocardial lesions in practically every one. Old latent syphilis is one of the most,

if not the most, important causes leading to myocardial incompetency; and, as the writer has said before, the latent syphilitic in the great majority of cases eventually dies a "cardiac failure" death. This may be brought about in several ways:

1. Myocardial atrophy and fibrosis due to slowly progressive mild syphilitic lesions in the myocardium. This is the most common form.

2. Syphilitic disease of the coronaries with resulting infarction and fibrosis.

3. Combination of these two processes.

4. Syphilis of the aortic valve. Always associated with some degree of myocardial syphilis.

5. Combination of myocardial syphilis and syphilitic mesaortitis.

6. Acute exacerbations of a previously latent syphilis ("critical stage" of syphilitic infection) or an acute malignant type of cardiac syphilis. This is much less common than the chronic latent form, but its frequency remains to be determined, as it has not received pathological recognition.

A CONSIDERATION OF THE PROGNOSIS IN SUBACUTE BACTERIAL ENDOCARDITIS*

E. LIBMAN, M.D., NEW YORK, N. Y.

THIS communication is based upon a study of over 800 cases of subacute bacterial endocarditis,† extending over a period of twenty-five years.[1] At first, this disease was supposed to be quite an unusual one, and the prognosis was regarded as practically uniformly hopeless. Even in 1910, our ideas concerning the outcome were quite different from what they are today. Since that time much new knowledge has been obtained concerning this remarkable disease and its end-results. I shall make a rather concise report, based mainly upon the cases which have come under my own observation, without detailing the various therapeutic methods which were employed. None of these latter has given a definite curative result.[2]

Inasmuch as the outlook of the disease depends upon the type of case, I shall present my studies under several headings. It is my intention to offer later one or more publications, in which each subdivision of the subject will be dealt with in greater detail. At that time I shall add the full clinical, therapeutic and anatomical data of my own cases as well as of those reported by others, and shall discuss more fully the criteria for the identification of the disease, especially in its less well-known forms, and for the prediction of recovery.

GROUP A. CASES OF UNUSUAL TYPE

In the form of the disease which has usually been recognized, running a course of from four to eighteen months or more, and characterized by fairly marked elevations of temperature, positive blood cultures and, usually, embolic phenomena, very few recoveries have been reported. Furthermore, in most of the published records of such cases the patients were observed for too short a time after recovery had apparently ensued.

In my first 150 cases of this type there were four complete recoveries, or three per cent. Since that time I have observed a number of other instances of similar favorable outcome. I refer now only to cases which have been kept under observation for a sufficient length of time, and in which no clinical residua or sequelae (not even embolism) have been demonstrable; excepting of course, the evidences of any previously

*From the Medical Department, Mount Sinai Hospital, New York City. Based on a presentation before the Association of American Physicians, Washington, D. C., May 6, 1925.

†The instances in which the aorta is the seat of a subacute bacterial infection and there is present only slight, or no involvement of the valves, are so few in number that they will not be included.

existing valvular defect. It is of interest to note that these patients did not even show any myocardial insufficiency beyond that which had been present before the infection took place. What the residua or sequelae of an attack of subacute bacterial endocarditis may be, will be described later in discussing the cases that came under observation for the first time in the so-called bacteria-free (healing or healed) stage of the malady.

Altogether, I have records of at least ten complete recoveries from the infection in the group under discussion. If I add those cases which recovered and later developed a fatal recurrence, the number becomes twelve. This does not include any case that came under observation in the bacteria-free stage, developed a recurrence, lost the infection, and continued with the symptoms of the preexisting bacteria-free stage. Of the twelve cases, three were of a type that can be classed as medium in intensity, as compared with the type under discussion, and with the mild type of the disease (see below). It is very probable that I failed to note instances of recovery after I studied the first 150 cases, because later the cases became so numerous, that not all could be accurately followed up for a proper length of time. There was no evidence that the various therapeutic methods that were employed were fully responsible for any of the recoveries, because the same methods were applied, without result, in many other cases.

Notes of a few of these instances of recovery will be of interest:

CASE 1.—Female patient, thirty-six years of age, observed since 1913.* The febrile period lasted at least three months. There was present a soft systolic apical murmur. Tender cutaneous nodes (Osler) appeared. On five occasions during the febrile period, the blood culture revealed anhemolytic streptococci (so-called *Streptococcus viridans*). The number of colonies in the first four cultures was 12, 85, 80 and 200, respectively. On the fifth occasion the cocci were demonstrable only in one of the flasks of bouillon. From that time (November, 1913) until December, 1924, ten blood cultures were made, all with negative results. The patient has meanwhile had an attack of typhoid fever. She is now suffering from hypertension, not of nephritic origin.

CASE 2.—Male patient, adult, observed since 1915. There was present an old valvular lesion, apparently of luetic origin. The febrile condition lasted, as far as could be determined, about one year, the temperature at times being as high as 104° F. Permission was only once obtained to make a bacteriological investigation of the blood. On that occasion a streptococcus of the anhemolytic variety was isolated. The patient suffered from no after-effects of the infection. He died in March, 1923, after suffering for a short time from cardiac insufficiency. A postmortem examination was not obtainable.

CASE 3.—Female adult, observed since 1913. There was present a soft systolic murmur, which did not appear to point definitely to an organic valvular condition. The febrile condition lasted for about two months. The blood culture revealed a streptococcus of the anhemolytic variety; the patient made a complete recovery. In 1914 she suffered from an attack of typhoid fever. She was seen by me in

*Through the kindness of the late Dr. Leon Louria, Dr. Simon R. Blattels, and Dr. S. J. Cohen, of Brooklyn.

February, 1917,—at which time she was in good health. The systolic murmur was no longer audible. Since that time, she has disappeared from observation.*

CASE 4.—Male adolescent, under observation with Dr. J. E. Reinthaler since May, 1917. He at that time suffered from an attack of subacute streptococcus endocarditis (blood culture positive) of a duration of at least three months. Valvular defects were present (aortic and mitral insufficiency). He was in good health until February, 1918, when he again had an attack lasting about three weeks. The blood culture was again positive. He made a good recovery, and at the present time has no complaints. The valvular defects have undergone no change.†

As is well known, there are cases of subacute bacterial endocarditis, having all the features of those in Group A, except the positive blood culture—at the postmortem examination of which, the vegetations are found full of bacteria. It is important not to confuse these with the cases designated as "cases in the bacteria-free stage." They are simply cases identical with those in Group A, except that the bacteria in the blood were not cultivated. In the series of cases reported in 1910 by Dr. Celler and myself,[4] which did not include any of the mild type of case, we obtained positive results in our blood cultures in 73 out of 75 cases. Later the percentage of positive findings at the hospital was not nearly as high. This was due mainly to the fact that the cultures were made by a succession of laboratory assistants having a short tenure of office, and to a less extent, I believe, to the fact that we began to recognize less pronounced forms of the disease than we had at first. Since Dr. Loewe has been making the cultures in most of our cases, and has been employing the methods which Dr. Celler and I applied, and also the Smith-Noguchi method (in a somewhat modified form) the percentage of positive results has been strikingly high. Other investigators have obtained very good results with the Rosenow technic. It should be employed in all cases in which negative results are obtained by other methods, and especially in the mild cases.

It would be of value to know the end-results of the lesions of the valvular and mural endocardium in the cases which have, under observation, made a complete clinical recovery. Fortunately all but one of my cases in this group are alive. In that one case, a postmortem examination was not obtainable.

The *cause of death* in the cases under discussion (Group A) is most commonly exhaustion. The myocardial weakness which may be present is usually of the type due to fever, anemia, and general weakness. At times, particularly if mitral stenosis be present, death may occur suddenly, preceded or not by hemoptysis (usually due to pulmonary infarction), or by a sharp attack of pulmonary edema. Embolism of a *coronary* artery is a rare terminal event—of a *cerebral* vessel, a

*Kindness of Dr. Josephine Walter who reported the case.[3]

†In subsequent communications there will be presented full notes concerning these and similar cases (occurrence of embolic phenomena, splenic enlargement, anemia, etc.).

quite frequent one. The patient may be carried off by gangrene due to embolism of a peripheral vessel. Other important causes are: polynuclear meningitis, subarachnoid and intraventricular hemorrhages, which are due at times to rupture of embolic aneurysms, rupture of such aneurysms situated elsewhere in the body, hyperpyrexia, and uremia. The last mentioned condition is uncommon in the cases which are still in the active, as compared to those in the bacteria-free, stage of the disease. A complicating pneumonia or an intercurrent or preexisting disease may carry off the patient. In some cases, it is a combination of various causes that is responsible for the fatal termination. A detailed analysis of this part of the subject will be made at a later time.

Of the cases that recovered completely from an attack, some, as stated above, have remained free from the infection. Recurrences will be described later. There are also cases in which the blood becomes free of bacteria, the fever disappears, but the patient succumbs after some weeks or months, during which time the clinical picture is that characteristic of the next group of cases.

GROUP B. CASES IN BACTERIA-FREE STAGE

There is a not inconsiderable number of cases that came under observation in the so-called bacteria-free stage. I published papers on this remarkable condition in 1912[5] and 1913,[6] giving the clinical, bacteriological and pathological findings.* At that time twenty-one such cases were described; since then I have observed many more.

In this group I refer to patients who usually present valvular defects and certain symptoms due to a previous attack of subacute bacterial endocarditis which was not clinically recognized (except for the occasional cases noted at the end of Section A). The blood cultures in such cases remain sterile, except for the very rare occurrence of a transitory bacteriemia which may arise in the course of any disease, and at the postmortem examination the vegetations, even when stained by special methods, show few or no bacteria. In patients dying in the active stage of the disease, the surface of the vegetations is packed with colonies of bacteria. When the number of bacteria is small, or when they are absent, the patient is going over to the bacteria-free stage, and the lesions are found to be healing. In a number of cases bacteria are no longer to be found and the lesions are healing or healed, as evidenced by fibrosis and often by calcification, which may be very extensive.

It must be remembered that in the depths of vegetations in even the most active cases healing is commonly observed. Sir William Osler noted this fact as early as 1885 (Goulstonian Lectures).[7] In what I have stated above, I refer particularly to healing of the super-

*The condition had been noted by Dr. Celler and me in 1910.[4]

ficial part of the lesions. It is the bacteria on the surface of the lesions that are thrown into the blood current and thereby keep up the fever and other toxic manifestations of the disease. When the lesions become bacteria-free, and even when they have undergone fibrosis or calcification, pieces may break off and plug vessels. In this way the embolic accidents of the bacteria-free stage arise (except for those due to thrombi in the left auricle, so commonly encountered in cases of mitral stenosis).

The proof that there exist spontaneously healing and healed cases of subacute bacterial endocarditis rests on pathological, bacteriological and clinical observations which I have elsewhere described and which need not be repeated here. A study of the transitional cases (next group to be described) has piled up the evidence. It is of interest to draw attention here to the hyperplasia of the pulp of the spleen, which is so remarkable an accompaniment of the healing endocardial lesions.

A number of authors have drawn attention to the spontaneous healing of the lesions of bacterial endocarditis. To Harbitz,[8] however, belongs the credit of having pointed out in 1897 and 1899, the spontaneous healing of the lesions in the disease which we now call subacute bacterial endocarditis. He stated that in ten cases which he believed to be related to chronic infective endocarditis, he found lesions characteristic of that disease, but containing no bacteria. There was extension to the walls of the auricle and ventricle, excrescences on corresponding parts of two adjacent flaps, and tearing of chordae tendineae. These cases ran a long course, at times associated with subacute nephritis. In a few instances indistinct groups of organisms were found in sections and smears but the cultures were negative. At the time at which Harbitz made his studies, the embolic glomerular lesion was not yet known, and he, therefore, could not make use of its presence in a healed form, as we did, to add the most important proof of spontaneous healing of the disease. The lesion of the commissures of the aortic valve described by Lewis and Grant is a valuable addition to our knowledge of healing (see Section F).

The cases in the so-called bacteria-free stage are essentially afebrile in character. Fever may be observed if the patient comes under observation in the transitional period, or if there be present marked anemia (anemic fever), large infarctions, or a complicating febrile condition. There is usually present a valvular defect and also one or more of the following manifestations, in varying combinations: a peculiar dark brown pigmentation of the face, renal insufficiency due to subacute or chronic glomerular nephritis, marked anemia, splenomegaly, embolism. Myocardial insufficiency is a much more marked feature than it is in the cases in the active bacterial stage.

A moderate enlargement of the spleen is practically always present, and tenderness of the lower sternum, very often. Petechiae and Osler nodes may appear, but less frequently and in much smaller numbers than in cases in the active stage. While Osler nodes are observed in almost 50 per cent of the latter (excluding mild forms of the disease), they were demonstrable in only three of twenty-one cases in the bacteria-free stage. I have found that the bacteria-free stage may last at least as long as two and one-half years; it is quite probable that at times it may last much longer than that. In 1917, with the kind assistance of Dr. Maurice Rashbaum, I made a study of the causes of death in twenty-seven cases in the bacteria-free stage, in which they could be fairly well determined. The data are as follows:

Myocardial insufficiency	5	cases
Myocardial and hepatic insufficiency	2	"
Myocardial insufficiency and pneumonia	1	"
Myocardial and renal insufficiency	1	"
Myocardial insufficiency and cerebral embolism	3	"
Myocardial insufficiency and tuberculosis and cerebral embolism	1	"
Myocardial and renal insufficiency and anemia	1	"
Renal insufficiency (uremia)	6	"
Renal insufficiency and cerebral embolism	1	"
Renal insufficiency, anemia, and pneumonia	1	"
Renal insufficiency and anemia	1	"
Cerebral embolism	3	"
Pneumonia	1	"

In this table anemia and pneumonia, when not the decisive factors, are not mentioned. They play a more important rôle than the table indicates. In the following summary the data are arranged in a way that shows more clearly the frequency of the most important causes of the fatal termination:

Myocardial insufficiency	was	a	determining	factor	in	14	cases
Renal insufficiency	"	"	"	"	"	11	"
Embolism (cerebral)	"	"	"	"	"	8	"
Hepatic insufficiency*	"	"	"	"	"	2	"
Anemia	"	"	"	"	"	3	"
Pneumonia	"	"	"	"	"	6	"
Tuberculosis	"	"	"	"	"	1	"

There were other occasional causes of death in cases in the bacteria-free stage, not included in this series of twenty-seven cases. The compilation makes very clear, however, the significance of renal insufficiency, anemia, embolism due to the fibrous tabs and calcareous masses left on the valves, and myocardial insufficiency. In a study made in 1922, by Dr. Benjamin Sacks and myself, it was found that uremia due to subacute or chronic glomerular nephritis was present in one-third of the cases in which the endocardial lesions had entirely healed.

*Apparent mainly secondary to the myocardial insufficiency.

The part played by myocardial insufficiency is striking. While the damage done to the heart muscle during the bacterial stage is no doubt a factor, it is probable that just as much or more significance is to be attached to the additional strain thrown upon it because of increase in preexisting valvular defects brought about in the process of healing.

When I first described these bacteria-free cases, it was stated that it was necessary to presuppose the existence of short and mild forms of subacute bacterial endocarditis in order to account for the fact that so often the patient passed through the stage of infection without its presence being recognized. The fact that Dr. Baehr[9] found a much smaller number of embolic glomerular lesions than in the patients dying in the active stage pointed to the same conclusion. This belief that such very mild forms of the disease would be encountered, as well as my preference for a designation based upon etiological rather than one based mainly on clinical considerations, were the reasons that I could not see my way clear to adopt the term "endocarditis lenta."[10]

Since the patients with positive blood cultures may make a complete recovery without clinical residua, and since we find patients in the bacteria-free stage who give no history of the active stage of the disease, we must take for granted the existence of cases in which the patient has suffered from an unrecognized infection of the endocardium and has recovered without any clinical residua or sequelae. Such patients might remain well indefinitely except for the consequences of a previously existing valvular defect (modified or not by the attack or attacks of subacute bacterial endocarditis) or of valvular changes produced by the latter (see below). We do know that a patient who is apparently in the bacteria-free stage, suffering from certain sequelae of the previous infection, may develop a recurrence, the outcome of which may or may not be favorable.

The use of the terms "bacteria-free" and "bacteria-free stage" to describe the cases in Group B is arbitrary. They are employed in referring to patients who have lost the infection, but in whom residua or sequelae are clinically manifest. The term "recovery" is applied in describing those patients who after withstanding the infection have no symptoms except those that may occur as a result of a previously existing valvular defect.

GROUP C. TRANSITIONAL CASES

Under this caption, I describe, for clinical convenience, certain cases which essentially belong in Groups A and B. These patients come under observation in different ways.

1. They appear with the symptoms of the active stage of the disease, and with positive blood cultures. The cultures soon become

negative and the patient recovers completely or presents the clinical picture of the cases in Group B.

2. The symptoms of the active stage are present but the blood culture is negative. The fever and other evidences of active infection disappear so rapidly that it is clear that the negative result of the blood culture was a correct finding. The outcome of these cases is like that in subgroup 1. They simply come under observation at a time still closer to the afebrile period.

3. The clinical features are essentially those of the bacteria-free stage, but other manifestations such as usually occur only in the active stage of the disease, as for example an abundance of petechiae in the conjunctival mucous membrane, together with the general appearance, make it appear probable that the patient was very recently in the active stage of the disease. In one case of this kind, the suspicion that the patient was just emerging from the infectious period was strengthened by the extraordinary observation made by the patient himself, that his fingers had become progressively more clubbed for several months, but that for a short time before coming under observation the clubbing had diminished.* As the patient was a tailor, and judged by the increasing and decreasing ability to wear his thimble, we readily credited his statement. The postmortem examination revealed some lesions which were in part still bacterial, but many more that were bacteria-free.

In our experience, it has happened that the transitional cases were fatal within a comparatively short time. There is no reason, however, why such patients might not survive for a long time, or even recover.

In the cases that come to postmortem examination while in the transitional period, the lesions are found completely or partially bacteria-free, and often partially healed. It not infrequently happens that in a case which is fatal during the active stage of the disease, the blood cultures still being positive, a great tendency to healing is found in parts of the vegetations. In other words, the lesion may be transitional, and the clinical picture still an active one.

GROUP D. MILD CASES

In recent years much has been learned concerning a mild form of the disease. The first important contribution to this subject was made by Oille, Graham and Detweiler,[11] who in 1915 described twenty-three cases of a subfebrile condition in all of which, by means of the Rosenow technic, anhemolytic streptococci were found in the blood.

*We do not know how often or to what extent the recession of clubbing occurs after the infectious stage of the disease has passed. For the present we must take it for granted that when this symptom is found we must make use of it cautiously for the diagnosis of subacute bacterial endocarditis, because it may be the result of a previous attack of the disease. Definite knowledge that the increase in size of the terminal phalanges is recent, is of much value.

Of five of the cases in which two to four blood cultures were made, three showed positive cultures at intervals of from three to four months. These patients all recovered from the infection.

In 1924 a further report was made by the same authors.[12] Three of the twenty-three cases could not be traced; the remaining twenty were known to be living; four were in good health, fourteen were fairly well and able to carry out their daily occupation, one was gradually losing strength and weight though still working as a music teacher, and one who had not worked for twelve years.

In 1920, Salus[13] of Prague, reported from the clinic of Funke a similar endemic occurrence of eighteen cases. The clinical data of these cases have unfortunately never been published. The cultural observations are detailed as follows: In ten cases blood cultures were made three times. In five of these the cultures were positive once, and in five others twice. In four cases cultures were made twice; in two, the result was positive once; in the other two, twice. In the remaining four cases, only one cultural investigation was made, and organisms were detected in each instance. As in the Toronto cases, Salus uniformly isolated an organism "corresponding to the Streptococcus viridans." He states that he does not believe that this organism is a sharply defined type, a view which is in agreement with the opinion expressed in 1910 by Dr. Celler and myself, and in recent years by Morgenroth and his pupils,[14] and by Kuczynski and Wolff.[15]

Capps,[16] Biggs,[17*] Major,[18] F. Janney Smith,[19] and others have described similar cases sporadically. I shall later analyze all the reports of such cases. It is important to do this because anhemolytic streptococci are being found with increasing frequency in the blood in cases of rheumatic fever, and because it has been found that such cocci may occur as transitory invaders in the course of other diseases. These organisms are not infrequently secondary invaders in medical and surgical diseases, and their rôle in a given case may be difficult to determine.[20]

I have had the opportunity of observing some of these remarkable cases. Such a mild infection may occur in an individual who presents no evidence of a previous attack of the disease, and who may or may not be the subject of an old valvular affection. On the other hand, it may occur in a patient who has for some time presented the clinical picture of the bacteria-free stage—just as a more severe type of infection may take place in such an individual. We will most likely find such mild forms as recurrences in patients who have suffered an attack of the disease of a more severe type, and who have made a complete recovery.

In these mild cases the rectal temperature may not rise to over

*The recoveries in Biggs' series of cases treated with cacodylate of soda were in the milder forms of the disease.

99.6° F. for weeks at a time. It may reach 101° F. and rarely 102° F. The patients are often up and about and may perform the duties of their occupation and take part in social activities. Marked embolic features are not likely to be encountered. If anemia is present it may or may not be marked. When it is marked, it is of assistance in making the diagnosis, as are also splenic involvement and the development under observation of clubbing of the fingers. It is also important to look sharply for tenderness of the lower sternum, white-centered petechiae, Osler nodes, meningismus,* and for macrophages (in the blood obtained from puncture of an ear). I cannot now go into a detailed description of the clinical features of this extraordinary condition, nor of the difficulties encountered in differentiating it from other conditions which it may simulate (tuberculosis, anemias, so-called neurasthenia, etc.). I wish however to emphasize the importance of keeping in mind the occurrence of mild forms of rheumatic fever in which blood cultures may yield a streptococcus of the anhemolytic variety. The greatest difficulty in diagnosis arises when a valvular defect is not demonstrable.

The blood culture is practically always positive at one time or another in these mild cases if the special methods to which I have referred are employed. As in the more marked forms of the disease, one does not always find a streptococcus. In one of my cases a Gram-negative diplococcus was twice recovered. Immunological aid is much needed for the clinical recognition of subacute bacterial endocarditis, particularly in the mild cases, and those in the bacteria-free stage.

It is difficult to estimate with precision the duration of subacute bacterial infections of the endocardium, and especially of the mild cases. While the latter appear to be essentially of rather short duration (occasionally as short as three weeks), they may last for quite a long time. I have observed one case that had a duration of at least six months, and another of at least one year. The most remarkable mild case which I have observed is that of a man,† now thirty years old, who has been ill since September, 1922, and under my observation since November, 1923. The duration of his illness, at the present writing (August 10), is almost three years, and the period of my observation, almost two years. Except for the short periods during which he suffers from pulmonary complications, his rectal temperature for weeks at a time does not rise above 99.4° F. He looks well, and has regained his full weight. The spleen is now just palpable, but has been larger. The valvular lesion is that of an aortic insufficiency (possibly also a congenital lesion). White-cen-

*This is a much neglected but valuable symptom of subacute bacterial endocarditis, of all degrees of severity, in the infectious period.

†This patient was presented at the meeting of the Association of American Physicians.

tered petechiae have been present, and for some time the sternum was very tender.

Since November 30, 1923, his blood has been cultured fifteen times, all of the examinations after the first one having been made by Dr. Loewe. The cultures that were positive showed anhemolytic streptococci by the ordinary aerobic methods as well as by the modified Smith-Noguchi method, except the last which was negative aerobically. The results were as follows:

November	30, 1923—	negative
December	18, 1923—	12 colonies to the c.c.
"	25, 1923—	20 " " " "
January	5, 1924—	38 " " " "
"	21, 1924—	12 " " " "
"	29, 1924—	35 " " " "
February	8, 1924—	25 " " " "
March	18, 1924—	1 " " " "
"	27, 1924—	2 " " " "
May	9, 1924—	200 " " " "
June	16, 1924—	18 " " " "
"	25, 1924—	50 " " " "
February	4, 1925—	8 " " " "
April	17, 1925—	positive only in modified Smith-Noguchi medium

We have been much surprised by the observations made on this patient, especially in finding a figure as high as 200 colonies to the c.c. of blood at a time when he was up and about, feeling well and having a temperature of only 99.2° F.

It is hardly necessary to dwell upon the significance of these mild infections which, I have no doubt, occur frequently. Henceforth we must entertain the possibility of the presence of this disease in patients suffering from the mildest subfebrile conditions which cannot be easily explained. In patients who are the subjects of old valvular lesions this consideration is most important. As the blood cultures may be positive when the elevation of the temperature is trifling, it will be of value to make them in patients suffering from valvular defects or congenital cardiac disease when they do not look well, appear anemic or unusually tired, or exhibit a change in the color of the face. Only by means of such investigations will we be in a position to ascertain the real frequency of subacute bacterial endocarditis and its influence on valvular disease. Such studies will be of less importance in patients who already present evidences of marked myocardial insufficiency, or who have developed auricular fibrillation, because we know, from clinical and pathological studies, that the disease is not apt to attack them.

All of the mild cases which I have recognized have recovered, except those which are still under observation and in which the illness has remained slight. I can say nothing definite concerning the pathological changes in them. In the course of anatomical studies of

hearts, however, one sees lesions of small extent which may very well represent the healing of mild infections. As already indicated, they may be responsible for some of the bacteria-free cases, especially those in which embolism is not a real feature, and in which the lesions in the heart are found to be moderate in extent. We do not know how much myocardial insufficiency may arise in these mild cases, due to the focal lesion in the heart muscle, characteristic of the disease. Nor do we know to what extent the embolic glomerular lesion occurs, nor how often a diffuse glomerular lesion may ensue.

GROUP E. RECURRENT CASES

In 1923, I drew attention to the fact that recurrence could take place in subacute bacterial endocarditis.[21] This subject is one of considerable importance. I shall however, on the present occasion, confine myself to a summary of the forms of recurrence which I have hitherto observed.

1. An attack of infection, a period of good health, a second attack, followed by good health.

2. Same as 1, but the second attack fatal.

3. An attack of infection, symptoms of the bacteria-free stage, followed by a second attack, with fatal outcome.

4. Symptoms of the bacteria-free stage, followed by an attack of the active disease, with fatal issue.

5. Same as 3, with recovery from the active infection, the symptoms of the bacteria-free stage persisting.

In other words, the patients may suffer two attacks, and recover or die; or the patient may come under observation afebrile in the bacteria-free stage, develop a fresh infection, and recover or die. The cases that I have seen, of the type described in subgroup 1 have not presented any clinical evidence of residua. There is every reason to believe that similar recurrences will be found, in which the patient manifests the clinical picture of the bacteria-free stage.

One of the recurrent cases is of so much interest that a few notes will be added here. The patient is a young man who was sixteen years of age when he came under observation in 1921, suffering from an attack of subacute bacterial endocarditis of average intensity. The illness apparently began with an attack of tonsillitis, on April 22. He had all the usual symptoms of the disease, including splenic enlargement, anemia, crops of white-centered petechiae, marked tenderness of the sternum, Osler nodes, etc. The examination of the heart revealed aortic and mitral insufficiency. The fever lasted until May 20. The blood cultures were negative (the newer methods were not used). The symptoms of the attack all disappeared, and the patient presented no evidence of infection for almost one year. On April

12, 1922, he again developed tonsillitis. He was admitted to the hospital on April 16, and discharged on May 25, 1922. He again presented the symptoms of subacute bacterial endocarditis, the elevation of temperature lasting until May 11. Two blood cultures were negative. On October 17, a tonsillectomy was performed. Except for minor ailments, he has remained well since that time and shows no after effects of the infections from which he suffered.

There is evidence that more than one recurrence may take place. In hearts obtained from cases of this disease, examples of recurrence are surprisingly common. Not infrequently one finds the lesions of an old healed attack accompanied by those of an active infection, or of an old healed attack and a healing attack, or of an older and a more recently healed attack. Sir Thomas Lewis, who from a survey of some of my specimens, found more confirmation of my clinical observations on recurrence than I had noted, has in his collection a specimen which shows the lesions of three distinct attacks. We shall probably find that there are cases in which the infection recurs at such short intervals that the condition becomes an almost continuous one, analogous to what one finds in certain cases of recurrent rheumatic endocarditis.

The discussion of the clinical recognition of recurrences will not be taken up now. It is interesting, however, to note that the presence of macrophages in the blood in a case in the bacteria-free stage, in which they were previously absent, may be of help in establishing the diagnosis of a recurrence. Occasionally one may be led to suspect that a patient is suffering from a recurrence if all the manifestations of an active infection are at hand but if at the same time the patient has the peculiar deep brown color of the face which occurs in the bacteria-free stage, but not in the active stage, of the disease.

There is evidence which indicates that repetitions of the infection may be due to an invasion from focal infections, as in the case cited above. It is of course possible that they may also be occasioned by invasion of the blood by bacteria deposited in various tissues during the previous attack (spleen, bone marrow, etc.). One might also conceive of reinfections arising from bacteria still remaining alive in the healing or healed lesions of a former infection. I doubt very much whether this conception is of any importance.

EFFECTS UPON THE VALVES

Because of the occurrence of healing and recurrence in subacute bacterial endocarditis, it is important to take up the subject of the effects of the disease on the valves themselves. There is an abundance of evidence proving that marked changes for the worse are not infrequently induced in previously existing valvular defects, and there are observations also which indicate that valvular defects may

be initiated. The results, apart from changes in the myocardium, which I have noted in the heart and aorta are, in brief, as follows:

Left auricle—small or large patches of thickening of endocardium.

Mitral valve—irregular fibrotic thickening, calcific deposits, aneurysm of the aortic flap, with or without perforation.

Chordae tendineae—tearing, more or less ulceration, fusion, knotting.

Papillary muscles—fibrous patches on the surface, especially at the tip.

Left ventricle—patches of thickening of endocardium, aneurysm in position of membranous septum, perforation in that location.

Aortic valve—more or less ulceration, fibrous thickening, calcific impregnation, projecting calcareous masses.

Aorta—aneurysm of the sinuses of Valsalva, and probably narrowing of the orifices of the coronary arteries.

The important lesions are those of the mitral cusps, the chordae tendineae, and the aortic valves. These clearly lead to increased insufficiencies and obstructions. It is not possible for me to answer definitely the question that has occasionally been put to me, as to the possibility of a mitral stenosis being produced by subacute bacterial endocarditis alone.

Of great significance in this connection are the lesions of the commissures, the presence of which was drawn to my attention by Sir Thomas Lewis. In the valuable paper dealing with the relationship of bicuspid aortic valves to subacute bacterial endocarditis, published by him and Grant,[22] there are illustrations of less marked forms of such lesions which they believe are the result of healing of the disease. While they have not advanced confirmatory evidence in the way of healed embolic glomerular lesions, I am convinced that their opinion is the correct one. The lesion of the commissures which is of the greatest interest is that type in which there is marked fibrous fusion of the flaps to each other and directly or nearly directly to the wall of the aorta. Such lesions are surprisingly frequent in the aortic valves of hearts which I formerly believed presented only the lesions of rheumatic endocarditis, or of atherosclerosis, combined with more or less marked fibrosis and often extensive calcification. Fusions of the cusps due to rheumatic endocarditis are of a different kind. It is advisable that all hearts which are the seat of valvular disease, especially of the aortic valve, be examined with reference to the various factors concerned in the pathogenesis of the lesions.

Apart from the rôle which these commissural lesions play in the development of aortic valvular defects, they afford additional evidence of the great frequency of healing of the lesions of subacute bacterial endocarditis. In some remarks[23] made in opening the discussion of a paper on this disease by Sir Thomas Horder at the

meeting of the British Medical Association in 1920, I stated that my studies indicated that between one-fifth and one-fourth of the patients suffering from a subacute streptococcus infection of the valves, spontaneously lose the infection. If we take into consideration the mild cases that we had overlooked, and the great incidence of healed lesions in the absence of a clinical history of the disease, this figure may well prove to be too conservative.

It must be evident that I have given only a general view of the prognosis in subacute bacterial endocarditis. Many other factors need consideration, such as the type and extent of preexisting valvular and myocardial disease, the influence of other diseases that may be present (such as tuberculosis, syphilis, etc.), and terminating infections. For a full presentation, it would be necessary also to discuss mixed infections of the valves and relationships with rheumatic fever, and to take up in detail the effects of the disease upon the various organs of the body.

While a remedy for the disease is a great desideratum, it is even more important that it be prevented. Even if we could overcome the infection, there is left the danger of anemia, nephritis, myocardial insufficiency, splenic disease, embolism, and increasing damage to the valves. As already indicated, even the mild forms of the disease which are so easily overlooked, or which may come under observation after they have lasted a long time, may cause valvular damage.

SUMMARY

If one were to be asked what knowledge we now have concerning the course of, and the prognosis in, subacute bacterial endocarditis, one could answer in brief, as follows:

1. There is a small number of spontaneous, complete recoveries in the type of case with which we first became acquainted.

2. There is a surprisingly large number of cases that come under observation with the sequelae of a former attack of the disease, either just before or directly after, the infectious stage has terminated, or, more commonly, without any clinical recognition of the attack.

3. There occur mild cases of short or long duration.

4. The disease may exist in recurrent form.

5. In the course of healing, the lesions of subacute bacterial endocarditis play a rôle in the development of chronic valvular disease.

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THE SELECTION OF PATIENTS WITH ANGINA PECTORIS FOR SYMPATHECTOMY; WITH A REPORT OF ADDITIONAL CASES*

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BOSTON, MASS.

DURING the past few years considerable attention has been paid to the clinical condition called angina pectoris, despite the fact that very little of importance has been added to the classical description of the disease as given by Heberden. In one respect much has been learned concerning the clinical recognition of a condition that has long been confounded with angina pectoris, namely, coronary thrombosis with cardiac infarction. Because of the greater familiarity with the disease, physicians are recognizing angina more commonly, and because of the decided increase in expectancy of life that has taken place in all parts of the civilized world the number of patients suffering from angina may actually have increased. It has also become clear to most physicians that a patient may be suffering from angina pectoris and yet complain of no real pain whatever. The symptom of slight tightness in the sternal region on walking, even in the absence of any physical abnormalities whatever on examination, may be all that the patient with angina will present. To this increased interest on the part of physicians there has recently been added, as a result of the work of Jonnesco,[1] a further impetus on the part of surgeons because an operation has been devised that attempts to bring relief to patients suffering from angina.

All new therapeutic procedures, especially for chronic illnesses, are first ushered in with a wave of enthusiasm and often die an early death after more prolonged and careful consideration. It may happen that, as a result of improper observations, even a therapeutic measure of value may be discarded. A brief review of the published cases of angina pectoris that have been operated upon will quickly convince the most skeptical that some of the patients have been greatly helped. On the other hand others have died on the day of the operation or shortly following it and some have not been helped at all. It is not our purpose here to discuss the rationale of the various procedures, although there is no unanimity of opinion as to the operation of choice. Successes and failures have followed excision of one or more of the cer-

*From the Medical and Surgical Clinics of the Peter Bent Brigham Hospital, Boston.

Read before the meeting of the American Heart Association, Atlantic City, N. J., May 26, 1925.

vical ganglia either on the left side or on both sides. Some have insisted that the depressor nerve alone should be resected, others have removed the stellate ganglion. Much more physiological investigation concerning the nerve supply of the heart and aorta in man and the underlying factors producing anginal attacks will be necessary before these points will be settled.

It is, however, most important that patients should be intelligently selected for operation if the treatment is to be given a fair trial. If the surgeon is to obtain whatever benefit sympathectomy may offer, he must either be entirely familiar with the methods of diagnosis or he must be dependent for the present on a physician who is competent to select the proper patient. It is obvious that diphtheria antitoxin will be of little use in Vincent's angina or membranous croup, although in both instances we would be treating a sore throat. Likewise all patients who have thoracic pain cannot benefit from sympathectomy for they are not all instances of angina pectoris. The diagnosis, in other words, must be exact. In an early communication one of us[2] emphasized the point that angina pectoris can be regarded as a distinct clinical entity although the underlying cause is somewhat disputed, much in the same way as we regard pernicious anemia as a clinical entity without knowing its exact cause. If one is thoroughly familiar with the condition it is possible to select, from those patients who have thoracic distress, a group called angina, in whom a certain course of events may be expected. Such prediction can be made with a fair degree of accuracy, not only as to the future clinical behavior of the patient, but in a large majority of instances as to the peculiar pathology that will be found at postmortem examination.

Angina pectoris generally occurs without any valvular disease, without congestive failure and even with a heart muscle that is essentially unchanged. When, however, there is evidence of valvular or muscular abnormality we are then dealing with a combined lesion of angina pectoris and something else, e.g., syphilitic aortic insufficiency. It is impossible to maintain that angina may exist without any pathological changes whatever in the heart, for in the great majority of cases autopsy reveals extensive coronary disease with infarction of the ventricles. However, during the time that the patient is ambulatory and suffering from the typical anginal attacks the coronary arteries may be damaged to no greater extent than is seen in other patients who have no angina.

For the present and until the rationale of the operation is worked out more thoroughly, there are two important points to be borne in mind in the selection of patients. In the first place the immediate operative mortality must be slight. Certainly caution is imperative in the development of any procedure and inasmuch as one cannot be

at all certain whether the operation is going to help, one ought to feel reasonably sure that it will not be damaging. Secondly, it should be our aim to select those patients who may be expected to live long enough to benefit from any satisfactory results that might follow the operation.

With regard to the former question it is necessary for us to distinguish attacks of angina pectoris from those of coronary thrombosis. Patients have been operated on who obviously, at the time of operation, were the victims of cardiac infarction following the occlusion of a coronary artery. There is no reason to believe, however optimistic one might feel as to the value of surgery for anginal attacks, that an operation is the proper procedure for this condition. That a patient may recover satisfactorily from such a grave condition with medical care is now well recognized, but such chances as exist may be jeopardized by subjecting him to the burden of a surgical operation. It, therefore, becomes necessary to distinguish the ordinary attacks of angina from those of coronary thrombosis. Much has been written about it and only a few distinguishing points will be taken up in this discussion.

In angina pectoris the sudden sensation of constriction, generally in the sternal region, coming on more particularly after walking, is momentary and can be relieved by nitroglycerin. In coronary thrombosis, on the other hand, the attack is more severe in character, lasts hours or days and is not relieved by the customary measures employed in anginal attacks. Moreover, in coronary thrombosis the pulse is apt to become rapid and frequently shows changes in rhythm; in angina it remains essentially unchanged. Then, too, the blood pressure is likely to rise during an anginal attack, whereas it almost always falls with thrombosis, and in the latter condition a fever and leucocytosis commonly occur. The differentiation is further clarified by subsequent events. Of particular importance are certain abnormalities shown on the electrocardiograms that indicate or suggest strongly that infarction of the heart is taking place. In short the clinical and laboratory data at our command suffice in most cases for an accurate differential diagnosis between angina and coronary thrombosis.

What has been said concerns the diagnosis, but prognosis is no less important in the selection of cases. If a patient shows evidence of myocardial damage sufficient to produce congestive heart failure, it is unlikely that he will be a good surgical risk, and it should not be forgotten that anginal attacks may spontaneously cease as congestive failure sets in, a fact which may explain some of the reported surgical successes. Furthermore, the coexistence of valvular disease must be duly considered. For although angina pectoris is uncommon in mitral stenosis (only one of 103 patients[2]) it is not so rare in the syphilitic type of aortic insufficiency—a progressive disease causing myocardial changes from which patients may die suddenly even in the absence of

congestive failure. Consequently patients with syphilitic aortic insufficiency should be operated upon for anginal attacks only as a last resort.

We consequently should employ every method at our disposal to estimate the condition of the myocardium before subjecting a patient with angina to a surgical operation. The favorable signs are a knowledge that the attacks come only on effort and not while at rest, that they are of short duration and that there has not been much shortness of breath. There should be no suspicion that cardiac infarction is taking place at the present moment or has occurred in the past. The vital capacity of the lungs should not be very much depressed and the electrocardiogram should show essentially normal complexes. It would be best if all the T-waves were upright and the QRS complexes sharp and of fair amplitude.

On examination the quality of the heart sounds should be good and this has particular reference to the first heart sound as heard at the apex. There should be no gallop rhythm or pulsus alternans. The rhythm should be normal. In this connection it is an interesting fact that practically all patients with angina pectoris have a regular heart rhythm, and despite the great frequency of auricular fibrillation with advancing years, it is very rare for a patient with this arhythmia to develop angina. There was only one such case out of 103 in a series recently studied.[2] The transient form of auricular fibrillation frequently accompanies infarction of the heart, but if the persistent form is present (and this is rare) there is probably an appreciable associated chronic myocarditis. The actual size of the heart is not of great importance as most patients with angina show only slight or moderate cardiac hypertrophy. Marked enlargement would indicate that grave myocarditis exists and should be a danger signal. The presence or absence of systolic murmurs has no practical significance, neither has the question of precordial hyperesthesia. The exact level of the systolic blood pressure is also of minor importance for it may vary from normal to an extremely high reading. One must bear in mind, however, that a very low pressure of 90 to 110 mm. may be the result of a previous infarction of the heart and demands an investigation from this point of view.

Applying the above criteria it is believed that the immediate surgical mortality for the operation will be insignificant and that the patients will live long enough to benefit from the results of the operation. Such has been the experience of the seven patients in whom we deliberately advised operation. They are all alive after intervals of from two years to three months after operation and all but one are improved. Four have no anginal symptoms at all, two have typical attacks of a nature milder than those previous to operation and one

is neither better nor worse. An eighth patient with syphilitic aortitis and aortic insufficiency was studied, and it was definitely decided that he should not be operated upon. He was treated medically in bed for ten weeks but the condition became aggravated and life became unbearable. The patient wanted the operation and although we were not inclined to advise it, it seemed likely that he would not live much longer under medical treatment. With this attitude perfectly clearly in mind, the operation was performed and the patient died several hours after it. This experience illustrates the points taken up in the discussion above. We suspected him of being a bad risk and autopsy showed an occlusion of the left coronary artery.

It is a striking fact that all seven patients who were deliberately selected not only survived the operation but are alive and with one exception are better months afterwards. It has been held by many that the abolition of the pain is undesirable, as the danger signal is lost and the underlying process left to progress even more rapidly. There is no evidence in favor of this view and with intelligent caution on the part of the patient it is unlikely that the increased activity will be harmful. In some instances a life that is slightly shorter but free from pain would be quite gratifying to the patient. In other instances when the sufferer cannot work it may render him self-supporting instead of a burden to others. It is, furthermore, not impossible that freedom from attacks actually retards the underlying process rather than accelerates it. Is it not conceivable that repeated spasms produce or speed up the coronary sclerosis that eventually leads to cardiac infarction and that when the operation is successful such a vicious circle is broken? Whether any effect is produced by surgery on the life expectancy of such patients, it will be impossible to state for some time to come; not until a large amount of data is compiled covering a longer span of years. There is no doubt, however, that some patients may be benefited in that the pain may be made to disappear or to become less distressing and the patient enabled to live in greater comfort.

Further progress in the selection of patients will also depend on intelligent study of the data underlying the various cases that have been operated on. It is urged that in reporting the results of such cases accurate and sufficient data as to the symptomatology and physical findings be given so that the reader might judge whether the patient truly had angina pectoris and whether there were other important factors that either indicated or contraindicated operative intervention. In that way it is felt that there will be practically no operative mortality and that we may be enabled to select those who give promise of enjoying relief for years.

REPORT OF CASES

CASE 1.—W. C. R., male, aged sixty years. Medical Number 21229. Surgical Number 18967.

Past History.—He had childhood infections and four attacks of rheumatic fever after the age of thirty-one.

Family History.—Not significant.

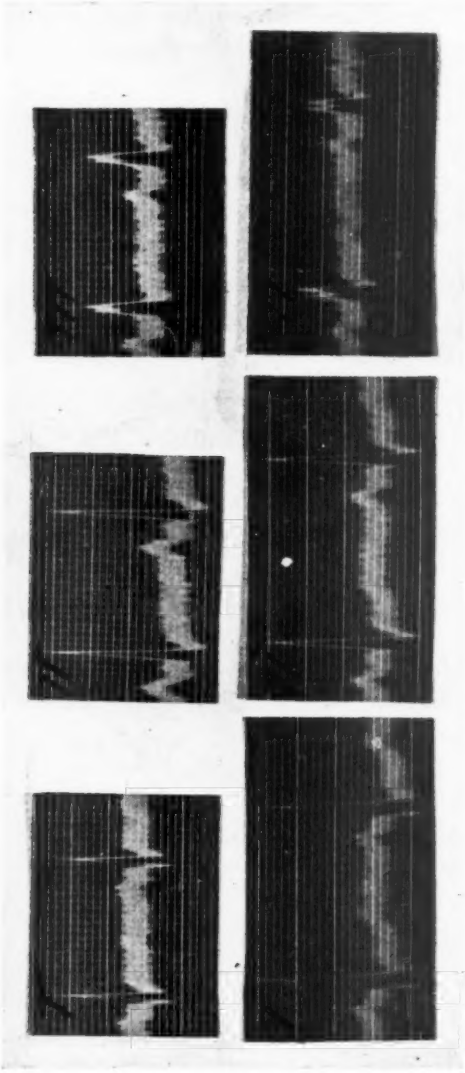

Fig. 1.—Case 1.—Upper tracing before operation (May 31, 1923). Lower tracing after operation (June 27, 1923). No digitalis given. Electrocardiograms are not particularly remarkable.

Present Illness.—For nine months he had attacks of retromanubrial pain on climbing hills, increasing in frequency. Two months before he was first seen he had a very severe attack beginning in the manubrium and radiating to the precordium and somewhat to the left neck but not to the arms. This was of a gripping, vise-like character "as if an iron band were being tightened up." The milder attacks would come more frequently on a full stomach or on stooping to tie his shoes. No

dyspnea. The patient distinguished two kinds of attacks, a milder one and a very severe attack which had been coming more frequently of late. These latter had been death-like and almost unbearable. Nitroglycerin was tried and found to relieve the attacks.

Physical Examination.—The patient had a large, easily reducible, right inguinal hernia. The rest of the examination was not abnormal. Radial and brachial arteries were slightly sclerosed. The heart was not particularly enlarged. The apex impulse was seen and felt in the nipple line 12 cm., to the left of the midline. Heart action was slow and regular. The first sound was of fair quality. No murmurs heard. No precordial hyperesthesia. No gallop rhythm or pulsus alternans. No signs of congestive heart failure. Blood pressure 132/90 mm.

Miscellaneous Data.—Vital capacity of lungs 3250 c.c. (75 per cent of normal). Wassermann negative. Electrocardiogram (see Fig. 1.) showed essentially normal curves. Urine was normal. X-ray of the heart (June 19, 1923) showed a normal sized heart. Transverse diameter 14.4 cm. Internal diameter of chest 27.5 cm.

Operation.—June 21, 1923. (Dr. E. C. Cutler.) Anesthesia, gas-oxygen. Left superior cervical sympathectomy.

Incision just anterior to posterior limit of sternocleidomastoid muscle from mastoid process to two inches above clavicle. Muscle split, exposing deeper structures. After segregation of the vascular bundle and identification of the vagus nerve the sympathetic chain was picked up and followed upward to the superior ganglion. Rami communicantes cut and ganglion avulsed from its cranial attachments. Two larger branches from the ganglion taken to be the sympathetic trunk to the middle ganglion and the superior cardiac nerve were cut near the ganglion. Closure with silk.

Postoperative Observations.—Immediately after operation Horner's syndrome (enophthalmos, contraction of the pupil and flushing of the face on the same side) appeared. He had some slight discomfort in the back of his ear from the scar. Otherwise he made a very good recovery. He was quickly able to walk about the hospital at a pace that was impossible before the operation. He experienced a slight sensation in the midsternal region on effort which was not particularly uncomfortable. Repeated electrocardiograms showed no significant change (June 27, 1923). Vital capacity of the lungs (June 26, 1923) 3100 c.c. (72 per cent of normal). The patient has been followed for two years since leaving the hospital. He has returned to work which he had to give up previously because of the pain. He has never had any severe attacks since operation, although typical mild attacks of angina on effort when climbing hills have persisted. The patient has repeatedly insisted that he feels a great deal better and that he can do more than before the operation without discomfort. These spells are still relieved by nitroglycerin.

Impression.—This patient was forced to stop work because of the increasing severity of attacks of angina. It seems that the operation gave him partial relief for although attacks continued they were milder in character and he was able to return to work.

CASE 2.—J. S., male, aged nineteen years. Medical Number 22566. Surgical Number 19763—A.

Past History.—At the age of ten he had rheumatic fever coming six months after tonsillectomy. He had frequent attacks, almost every spring, following this.

Present Illness.—For several years he had attacks of palpitation and pain in the center of the chest in the midsternal region radiating to the back down to neck or arms and always relieved by nitroglycerin. There was slight dyspnea on exertion but this was not so troublesome as the pain which at times was agonizing. There was in addition more recently a different pain described as an ache in the region of the apex of the heart. The attacks of sternal pain came frequently and continued

for a while even after rest in bed, although prolonged medical care generally caused a diminution in the frequency and severity of the attacks. Latterly the pain took on a constricting character and radiated both to the right neck and to the left axilla. He was treated on the medical wards of the Peter Bent Brigham Hospital for intervals of several weeks at a time during the years 1921, 1922 and 1923.

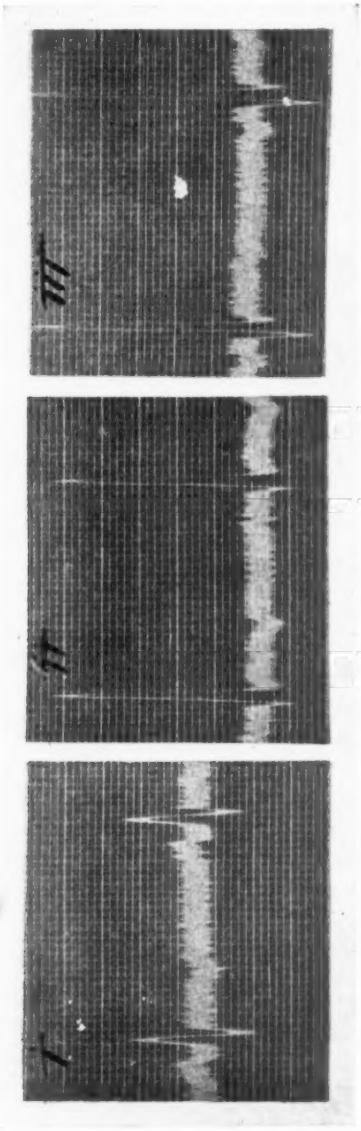

Fig. 2.—Case 2.—Electrocardiograms taken before operation (December 21, 1922). No digitalis given. The T-waves are rather flat in all leads.

Physical Examination.—The patient presented the picture of typical advanced rheumatic aortic insufficiency with possibly some mitral involvement as well. The heart was tremendously enlarged. The apex was felt in the seventh intercostal space in the midaxillary line. The action was regular and generally about 80 to the minute. There was a loud systolic murmur all over the precordium and a blowing aortic diastolic murmur at the base and along the left sternal border.

There was no peripheral edema; the liver was not enlarged and there was no congestion of the lungs. Blood pressure was 160 mm., systolic, diastolic 0. The peripheral arteries pulsated violently.

Miscellaneous Data.—Vital capacity of the lungs 2700 cc. (67 per cent of normal). Phthalein test 65 per cent. Blood Wassermann negative. Urine showed a slight trace of albumin, no sugar, and the sediment showed a rare hyaline cast. Stools negative. Hemoglobin 100 per cent. Red blood count 5,100,000. White blood count 11,000. Stained smear normal. Electrocardiograms showed slightly inverted T-waves in Leads I and II. (See Fig. 2.) X-ray of the heart (Sept. 28, 1923) measurements—right border 4.7 cm. and left border 13.1 cm. from midline. Great vessels 5 cm. Internal transverse diameter of the chest 27.7 cm.

Patient ran no appreciable fever, but palpitation and frequent attacks of chest pain remained troublesome. Inasmuch as the boy had been unable to work and had not shown signs of congestive heart failure it seemed that should a sympathectomy relieve him of the pain, this might render him self-supporting. We clearly recognized that we were dealing with angina pectoris complicating rheumatic aortic insufficiency, but inasmuch as the life expectancy might be a considerable number of years an operation for the possible relief of pain itself seemed justifiable.

Operation.—Oct., 3, 1923. (Dr. E. C. Cutler.) Anesthetic—ether. Left superior cervical sympathectomy.

Usual incision along edge of sternomastoid muscle carried through to exposure of the vascular bundle. Latter raised and cervical trunk of sympathetic identified. The ganglion was avulsed from its cranial attachment after cutting with scissors the numerous rami communicantes. The trunk below was then divided below the branching of the superior cardiac nerve. Closure with silk.

Postoperative Observations.—There was left enophthalmos with a dilated right pupil and injection of the left conjunctiva with marked sweating on right side of face but none on the left the day after operation. A peculiar herpetic eruption developed over the left ear and neck of pustular character. Patient was observed for two weeks and anginal attacks seemed to come with about the same frequency and severity as before operation. In view of this fact a second operation, this time on the right side was advised.

Operation.—Oct. 18, 1923. (Dr. E. C. Cutler.) Resection of fragment of right superior cardiac nerve and ramus communicans from middle and superior ganglia.

Postoperative Observations.—Patient had numerous attacks of pain during which it was frequently found that the blood pressure rose to 250 mm. Following nitroglycerin the attack would subside with accompanying fall in blood pressure. The attacks gradually diminished in frequency and the patient was discharged with advice to use nitroglycerin for his attacks.

September 12, 1924.—Patient had been working daily for several months and complained of attacks of throbbing and pounding in right axilla. The sensation was of a tight feeling under the arm. They were not related to effort but would be precipitated by emotion and excitement. He had no pain in chest or left arm at all. He felt more nervous than before the operations and complained of a pumping sensation in the left cheek on eating. Physical examination at this time was essentially the same as before operation except for persistent bilateral enophthalmos.

August, 1925.—Condition remains the same.

Impression.—On the whole the patient felt that the operation had benefited him to the extent that he no longer had attacks of chest pain.

CASE 3.—C. F. W., male, aged seventy-two years. Surgical Number 20,451.

Past History.—Always been well up to time of present illness except for minor troubles. No rheumatic affections. He had scarlet fever at the age of two years and ever since then has had a lateral tremor of his head.

Family History.—Not significant.

Present Illness.—For three years the patient had noticed a pressure sensation in midsternum on walking or bicycling strenuously. He had to stop to relieve this. When he was taken with these spells he became immobile and was afraid to breathe. They came with increased frequency and occasionally he noticed a rheumatic pain in the left arm. There were often associated with these attacks a feeling of nausea and occasionally vomiting. Nitroglycerin was tried and found to relieve these attacks.

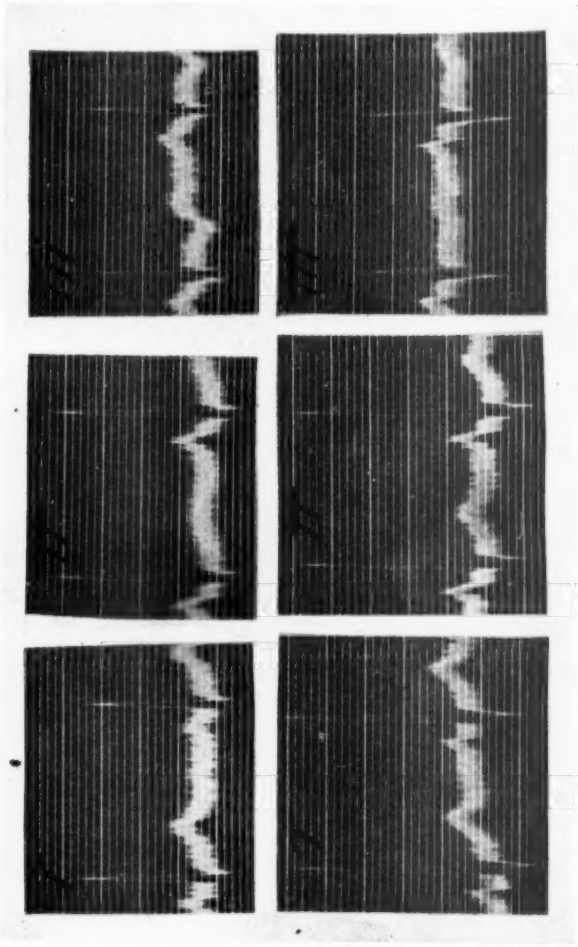

Fig. 3.—Case 3.—Upper tracing before operation (January 5, 1924). Lower tracing after operation (January 15, 1924). No digitalis given. The T-waves in Leads II and III became somewhat more upright.

Physical Examination.—Not particularly remarkable except for the heart. Radial and brachial arteries moderately sclerosed. The heart was definitely enlarged. Left border was 2 cm. outside the nipple line. Action was slow and regular, with occasional premature beat. A slight systolic murmur was present at apex and base. No diastolic murmur was heard. The first sound was of good quality. No gallop rhythm or pulsus alternans. No signs of congestive heart failure. Blood pressure 172/74.

Miscellaneous Data.—Vital capacity of lungs 2225 c.c. (60 per cent of normal). Wassermann negative. Electrocardiogram (see Fig. 3) January 5, 1924, showed

essentially normal curves. Urine was normal except for frequent white blood cells in sediment. Phthalein 65 per cent. Blood cells were normal. X-ray of the heart showed moderate cardiac enlargement. Transverse diameter of the heart 13.9 cm. Internal diameter of chest 25 cm. (January 5, 1924).

Operation.—January 7, 1924. (Dr. E. C. Cutler.) Anesthesia—ether. Cervicothoracic sympathectomy.

Usual incision along the edge of the sternomastoid muscle, edge being split and muscle retracted toward the midline. Neurovascular bundle and vagus nerve identified. The superior cervical sympathetic ganglion was picked up, all ramifications cut, upper end avulsed from the base of the skull and the cervical sympathetic trunk then followed downward. The middle ganglion was then encountered and below this the inferior ganglion. All connections were cut and the chain removed. Closure with silk.

Postoperative Observations.—Immediately following operation there appeared a typical Horner's syndrome on the left side. A reexamination of the heart by x-ray (January 14, 1924) showed no appreciable change. Electrocardiograms (January 15, 1924) were essentially the same as before the operation. Patient was discharged from the hospital nine days after operation and he has been followed for one and a half years. On June 12, 1924, his blood pressure was 160/80 mm. and vital capacity of lungs 2100 c.c. There has been a considerable amount of pain and discomfort in the left side of the neck and face, and some difficulty in chewing. The pain of constriction in the sternal region coming on effort was present for some months. This could be relieved either by resting or taking nitroglycerin. It was distinctly less troublesome. Both the patient and his wife were quite insistent as to this. During the past year, however, there has been no angina whatever, although the discomfort in the face has persisted. He is now able to walk much more than formerly. (August, 1925.)

Impression.—It is quite clear that the patient continued to be troubled with anginal attacks for several months after the operation. They were much less severe and it took greater effort to bring them on. Gradually they all disappeared and for a year he has had none whatever.

CASE 4.—F. M. S., male, aged sixty-one years. First seen January 10, 1924.

Past History.—Patient had always been a well, strong man. No important illness. No rheumatic infections.

Family History.—Father died at seventy-five of angina pectoris. One brother died of "heart trouble" at sixty-three years of age.

Present Illness.—Four or five years previously he had a feeling of pressure and feeling of constriction across the middle of the chest. He never had this recur until December 20, 1923. On this day while walking up a little hill he experienced a disagreeable clutching sensation in the middle of his chest which made him stop. This passed off in five or ten minutes. Since then similar attacks had recurred with increasing facility so that finally he was unable to walk a block even on the level without a spell. With this there has also been an ache in the left elbow and along the inner surface of the left arm. He had been helped with nitroglycerin. Recently the effort of undressing at night or exposure to cold air precipitated attacks. In 1918 his blood pressure was known to have been 170 mm.

Physical Examination.—Essentially normal except for the cardiovascular system. Heart was somewhat enlarged. Action was regular. First sound at apex was slightly diminished in intensity and followed by a moderately loud systolic murmur. A fainter systolic murmur was heard at the base. No diastolic murmur heard. Aortic second sound accentuated. Radial and brachial arteries somewhat sclerosed. Blood pressure 190/106 mm. No pulsus alternans. No signs of congestive heart failure.

Miscellaneous Data.—Vital capacity of lungs 2950 c.c. (67 per cent of normal). Wassermann negative. Electrocardiogram (see Fig. 4), showed slightly diphasic T-waves in all leads. Urine was normal. *X*-ray of the heart showed slightly prominent aortic arch which measured 5.9 cm. in diameter. Transverse diameter of heart was 12.6 cm. Internal diameter of chest 27 cm.

*Operation**.—Jan. 20, 1924. (Dr. H. Lilienthal.) Left superior and middle cervical sympathectomy. Anesthesia—nitrous-oxide and ether.

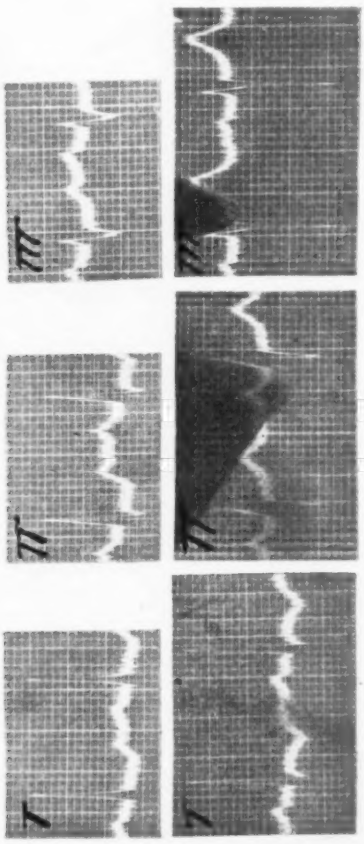

Fig. 4.—Case 4.—Upper tracing before operation (January 10, 1924). Lower tracing after operation (February 19, 1924). No digitalis given. The T-waves became more upright in Leads II and III and S-waves more marked in the same leads.

Dr. Lilienthal's Operative Note.—Through an incision along the border of the left sternocleidomastoid muscle about four inches in length the dissection was made exposing the neurovascular sheath and the deep muscles of the neck. No external jugular was present and it was somewhat embarrassing to find that the internal jugular was also absent, its place being taken by the vertebral vein. The vagus was seen but not disturbed. The sympathetic nerve was identified by its middle ganglion and followed up to the superior which lay behind the internal carotid artery. Its tributaries were divided with scissors and the ganglion avulsed from its cranial attachment. It was fully one-half inch in length. The nerve was cut below the middle

*This case has been previously reported by Dr. H. Lilienthal of New York, Arch. Surg., Jan., 1925, x.

ganglion. The wound was closed with temporary drainage to get rid of the immediate outflow of serum. Horner's syndrome was at once observed.

Postoperative Observations.—The patient has been seen repeatedly for eighteen months since the operation. He has never had an attack of angina during this time. There has been some troublesome paresthesia in the left side of face, neck and clavicle. He has been able to increase his activities so that he could walk two to five miles without distress. Against advice he has lifted heavy weights and has gone hunting without any apparent ill effects.

Miscellaneous Data.—General examination remains essentially unchanged. Blood pressure has ranged between 150 and 180 mm. systolic and 80 to 98 diastolic. Vital capacity of lungs 2800 c.c. (62 per cent of normal).

Impression.—This patient has made a remarkable symptomatic recovery following operation. He repeatedly has stated that he feels as well as he has for many years.

CASE 5.—J. B. T., male, aged seventy-one years. Surgical Number 22807.

Past History.—Essentially negative. No rheumatic infections.

Family History.—Unimportant. One brother said to have died of "heart trouble."

Present Illness.—Patient has had two different types of complaints. For two years he has had a feeling of tightness or pressure in the region of the manubrium only on effort, never while resting. This feeling was slightly to the left of the sternum and could always be controlled by rest. A walk of 50 to 100 yards would generally precipitate one of these attacks. In addition he has had a different sensation which he described as a tremendous pressure in the upper sternum lasting five to ten minutes coming only after meals on three occasions and promptly relieved by nitroglycerin. Otherwise he has felt very well. There has been no dyspnea. Up to two years ago he was able to play tennis. He has occasionally had a little palpitation of the heart at night.

Physical Examination.—Patient was a very well preserved, intelligent, elderly man. General physical examination essentially negative. Heart was not enlarged. Action was slow. Rate averaged 60 per minute. There was a sinus arhythmia. Heart sounds were of fair quality. No murmurs were heard. The radial and brachial arteries were markedly sclerosed and tortuous. There were no signs whatever of congestive heart failure. Blood pressure 138/74. No pulsus alternans.

Miscellaneous Data.—Vital capacity of the lungs 3700 c.c. (90 per cent of normal). Wassermann negative. Electrocardiogram (see Fig. 5) essentially normal. Urine was negative. Blood normal. X-ray of the heart was negative. Transverse diameter 13.8 cm. Internal diameter of chest 30.2 cm. (December 16, 1924).

Operation.—December 17, 1924. (Dr. F. C. Newton.) Left superior cervical sympathectomy. Anesthetic—ether.

Usual incision along the edge of the left sternomastoid muscle carried through muscle fibers to deeper structures. The vascular bundle was identified and raised gently toward the midline. Vagus nerve identified. Sympathetic trunk segregated and followed upward to its fusion in the bulbous superior cervical ganglion. Rami communicantes cut and the ganglion avulsed from its cranial attachment. The chain was then followed downward to a point below where the superior cardiac nerve branched off and both nerves cut about one-half inch below this juncture. Closure with silk.

Postoperative Observations.—Directly after operation there was the usual typical Horner's syndrome on the left. The patient has been followed for eight months. During this time there has never been a single attack of angina pectoris since the day of operation. From time to time he has complained of pain in the left shoulder and left side of his face. One week after operation he was walking about and recently (June, 1925) has been able to walk two miles without discomfort. General

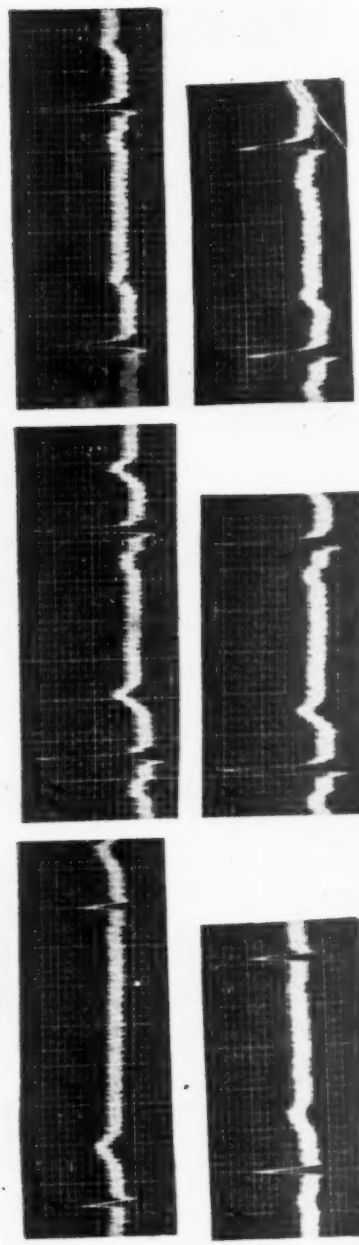

Fig. 5.—Case 5.—Upper tracing before operation (December 2, 1924). Lower tracing after operation (April 29, 1925). No digitalis given. No particular change is evident.

physical examination has remained unchanged. Blood pressure shortly after the operation (December 22, 1924) was 110/66 mm. This has since returned to the pre-operative level of 138/80. Occasional premature auricular beats have been present both before and after the operation. Electrocardiograms have remained essentially unchanged. Vital capacity of lungs (June 15, 1925) 3700 c.c.

Impression.—This patient has made a most satisfactory symptomatic recovery as a result of operation. Whereas formerly he was unable to walk and was restricted in his activities he now enjoys comparatively good health.

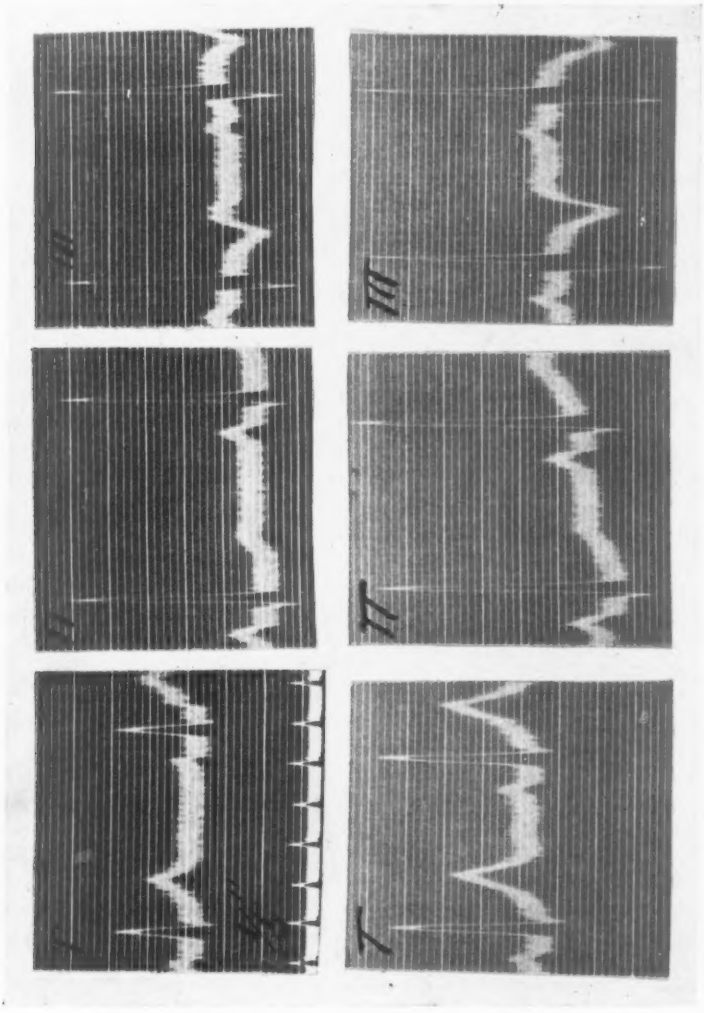

Fig. 6.—Case 6.—Upper tracing before operation (January 30, 1925). Lower tracing after operation (February 24, 1925). No digitalis given. All complexes were slightly increased.

CASE 6.—S. N., male, aged forty-nine years. Medical Number 25218. Surgical Number 25128.

Past History.—No rheumatic fever, chorea or venereal disease. Has always been a strong, vigorous man.

Family History.—Not significant.

Present Illness.—Nine months before admission to the hospital he was seized while at work with a sharp pain over the heart extending down the left arm to the

wrist. It was accompanied by a feeling of constriction beneath the sternum. The pain lasted one hour. He then felt well until two weeks later when a similar attack returned on exertion. In some of these attacks there was radiation to the right as well as to the left. Since then the attacks had come almost daily, especially in the morning after breakfast. Nitroglycerin had given him some relief. December 25, 1924, he had a severe attack of pain lasting one and a half hours with gradual recovery. The description of the attack suggested the possibility of a small coronary thrombosis.

Physical Examination.—Essentially normal except for the heart. There was no cardiac enlargement to percussion and no precordial hyperesthesia. Action slow and regular. First heart sound was definitely diminished in intensity. No murmurs were heard. No evidence of congestive heart failure. Radial and brachial arteries were moderately sclerosed. No pulsus alternans. Blood pressure 120/70 mm.

Miscellaneous Data.—Vital capacity of lungs 4100 c.c. (93 per cent of normal). Wassermann negative. Electrocardiograms are normal except for a sharply inverted T-wave in Lead III. (See Fig. 6.) Urine examination was normal. Phthalein 69 per cent. Blood was normal. X-ray of heart showed transverse diameter 14.1 cm. Internal diameter of chest 30.2 cm.

Operation.—February 9, 1925. (Dr. F. C. Newton.) Anesthetic—ether. Left superior and middle cervical sympathectomy.

The operative procedure followed in this case was identical with that of Case 5. The ganglion presented, however, somewhat different characteristics. It was thicker and more chunky than usual, at least 6—7 rami communicantes were cut and the ganglion avulsed from the cranial attachment. It was followed downward to a point where the three branches which left the ganglion converged again into a second definite bulbous enlargment taken to be the middle cervical ganglion. The trunk and two branches below this were followed still lower and cut. Closure with silk.

Postoperative Observations.—There was only very slight evidence of Horner's syndrome present following operation. Five days after operation the patient was allowed out of bed and to walk more and more. It quickly became apparent that he could walk a distance without pain which was impossible before the operation. He did complain of pain in the left shoulder and tightness in the left side of the neck not related to effort. This has been commonly seen as a result of nerve stretching at time of operation. February 12, 1925, blood pressure 112/70 mm. Repeated x-ray plates of the heart showed no appreciative change (February 24, 1925). Electrocardiogram tracings remained the same as before operation. A few weeks after discharge from the hospital the patient resumed his former activities, a thing he had not been able to do for three months previous to operation. He has been troubled by his left shoulder and there has been an occasional ache in the region of the left nipple not of anginal character.

Impression.—The result in this case was gratifying. A man who had to support himself and who was incapacitated from work because of anginal pain became free from attacks following operation and was restored to economic independence and at present (July, 1925) is still free from attacks.

CASE 7.—A. M., male, age forty-nine years. Surgical Number 23512.

Past History.—No rheumatic fever or chorea. Many sore throats until tonsillectomy eighteen years ago. Gonococcus infection twice, at age of seventeen and again at 30. Negative history of lues. Use of tobacco has been excessive; as much as 40 cigarettes and 8 cigars a day.

Family History.—Father died of angina at sixty-seven. Mother is living and well at seventy-one. One brother has diabetes at thirty-nine. One sister has "heart trouble" at thirty-four.

Present Illness.—For eight years the patient had attacks of pain either in left arm or in the center of his chest on walking, especially if he walked directly after meals. Sometimes this feeling, which he called a steady ache, began in both arms and then involved the chest between the two nipples. At other times it was only in the chest. It was quickly relieved upon resting. He stated that if he could belch gas it would relieve him. The discomfort lasted two or three minutes. On two occasions attacks had awakened him from sleep. He never had been short of breath

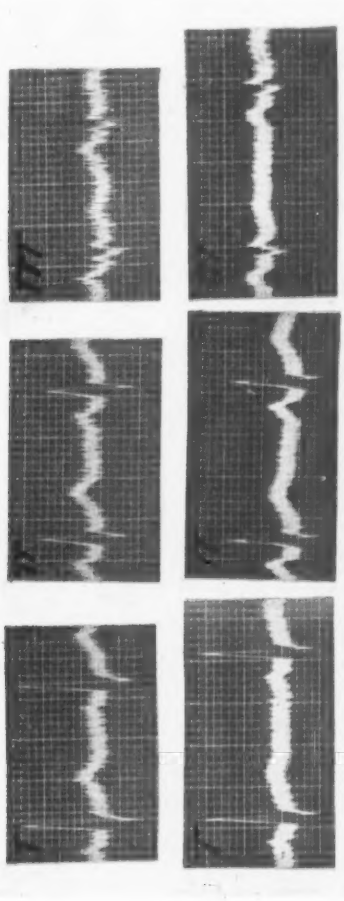

Fig. 7.—Case 7.—Upper tracing before operation (March 24, 1925). Lower tracing after operation (May 28, 1925). No digitalis given. No essential change.

and otherwise he felt very well. His main difficulty was that he could not walk on account of these spells. He never used nitroglycerin.

Physical Examination.—Complete physical examination essentially normal except for the heart. This showed slight enlargement, 1.5 cm. outside the nipple by percussion. The heart action was slow and regular. The first sound as heard at the apex was of fair quality. There was an apical and a basal systolic murmur. No diastolic murmur. Radial and brachial arteries slightly sclerosed. Blood pressure 170/90 mm. No pulsus alternans.

Miscellaneous Data.—Vital capacity of lungs 3200 c.c. (77 per cent of normal). Wassermann negative. Electrocardiogram essentially normal. (See Fig. 7.) Urine was negative except for a rare hyaline cast. Blood was normal. X-ray of the

heart showed a moderately tortuous aorta not dilated. Transverse diameter of the heart was 13.8 cm. Internal diameter of chest was 28.0 cm. (March 27, 1925).

Operation.—March 30, 1925. (Dr. F. C. Newton.) Left superior cervical sympathectomy. Anesthetic—ether.

Usual incision along external edge of sternomastoid muscle, carried along to the deeper structure. The vascular bundle was identified and pulled toward the midline gently. Vagus nerve seen and retracted. The sympathetic nerve, lying below this group of structures was then picked up and followed upward until it merged into the superior cervical ganglion. After carefully cutting the rami communicantes the ganglion was then avulsed from its cranial attachment. The sympathetic trunk was then followed downward to a point below the branching of the superior cervical nerve and both cut. Closure with silk.

Postoperative Observations.—Patient had a typical enophthalmos and contracted pupil, with moderate amount of injection of conjunctiva. Reexamination of the heart by x-ray showed a decrease of 1 cm. in the transverse diameter (April 6, 1925). For a few days patient was able to walk up two flights of stairs and for considerable distance on the level without attack of pain. Later, however, he noticed his old discomfort returning, now localized to the center of the sternum. It was, therefore, decided to perform a similar operation on the right side.

Second Operation.—April 9, 1925. (Dr. F. C. Newton.) Right superior cervical sympathectomy. Anesthetic—ether.

Identically the same procedure carried out on the right side as that outlined above for the left.

Postoperative Observations.—This resulted in a right-sided enophthalmos which restored the symmetry of the face. He remained free from attacks and was able to walk distances that were formerly impossible for a period of about two weeks after the last operation. Subsequently typical attacks returned of the same character as before the operation but of less severity. These spells have since been considerably helped by medical supervision following the administration of diuretin and erythrol tetranitrate. Four weeks after he left the hospital there developed some pain and discomfort on motion in the region of his shoulders for which he received baking and massage. September, 1925. He now has practically no attacks and can walk two miles.

Impression.—In reviewing the result obtained in this case it seems that little if any good was accomplished by the two operations, although subsequent medical treatment has greatly helped.

CASE 8.—D. McG., male, aged fifty-one years. Medical Number 23812. Surgical Number 21891.

Past history.—No rheumatic infections. Primary luetic lesion 20 years previous with secondary manifestations. Used alcohol to excess.

Family History.—Not significant.

Present Illness.—For four months the patient had increasingly severe attacks of gripping pain in the chest. They were burning and choking in character, beginning in the epigastrium and extending up the sternum and sometimes into the left arm. They would last about ten minutes and then gradually pass away. They occurred almost daily, at first brought on by the slightest exertion or by eating, and later waking him from sleep. They were so agonizing that he felt as if he were going to die. The pain was usually associated with dyspnea, a choking sensation and palpitation of the heart. The attacks were generally relieved by nitroglycerin.

Physical Examination.—Essentially negative except for the circulatory system. The peripheral arteries were throbbing prominently. The heart was slightly enlarged, action regular. A soft systolic and diastolic murmur could be heard at the apex and these became louder on approaching the base. No peripheral arteriosclerosis and no signs of congestive failure. Blood pressure 140/0. mm.

Miscellaneous Data.—Vital capacity of lungs 3300 c.c. (75 per cent of normal). Electrocardiograms (see Fig. 8) showed inverted T-waves in Lead III and slight slurring of QRS complex. Wassermann double plus. Phthalein test 35 per cent. Urine normal. Blood normal. X-ray of heart (June 23, 1924) showed moderate widening of the aortic shadow, 8.0 cm. Transverse diameter of the heart 14.2 cm. Internal diameter of the chest 29.5 cm.

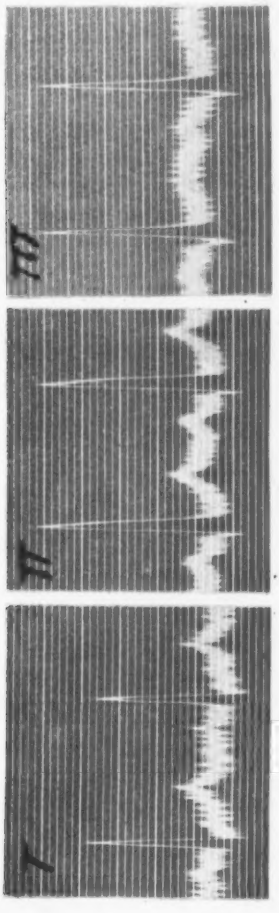

Fig. 8.—Case 8.—Upper tracing before operation (June 30, 1924). There was a slight slurring of the QRS complex. No digitalis given.

Subsequent Notes.—Patient was regarded as suffering from luetic aortitis and angina pectoris. At the onset the possibility of a sympathectomy was taken up and it was decided, because of the valve disease and syphilitic process and the fact that attacks kept recurring even without effort that this patient was not a suitable case for surgical treatment. He, therefore, was kept on the medical wards in bed for ten weeks. He first received mercury intramuscularly and increasing doses of saturated solution of potassium iodide. Later he was given weekly small doses of arsenobenzol intravenously. Despite the active antiluetic treatment typical attacks of angina persisted with great frequency requiring nitroglycerin for relief. The patient was no better and inasmuch as he had been unable to work and the outlook

for recovery was otherwise hopeless we finally consented to advise operation, realizing that the risk was great.

Operation.—August 13, 1924. (Dr. D. C. Cheever.) Left superior, middle and inferior cervical sympathectomy. Anesthesia—ether.

Usual incision along mesial border of sternomastoid muscle, carried through to deeper tissues. Vascular bundle identified and retracted inwards. Superior cervical ganglion picked up and traced upward to its cranial attachments. Avulsed after all communicating rami were cut. Trunk followed downward to merge in the mid-ganglion and below this to the inferior ganglion. All branches to these were cut and the nerve chain removed. Closure with silk.

Postoperative Note.—The patient made the usual immediate recovery after operation. He was free from pain. Horner's syndrome was present. Five hours after operation he was found dead in bed a few moments after being seen in satisfactory condition.

Postmortem Examination.—Heart was somewhat enlarged weighing 420 grams. There was evidence of syphilitic aortitis with aortic insufficiency. The left coronary artery was occluded at its origin.

Impression.—It was originally decided after reviewing all the details of this case that this patient was unsuitable for surgical treatment. He was, therefore, not deliberately selected and operation was finally done merely because medical treatment had failed and his outlook appeared hopeless. The fatal outcome emphasizes the very points in our discussion relative to the proper selection of patients.

SUMMARY

1. Some patients suffering from angina have been strikingly helped by cervical sympathectomy.

2. A proper selection of cases ought to diminish markedly the immediate surgical mortality, and this selection should be so directed that those who are operated upon continue to live for an appreciable length of time to enjoy their improved health.

3. It is absolutely necessary that accurate diagnoses be made and that cardiac infarction be not confounded with angina pectoris. Furthermore the study of each patient should indicate that there has not been any congestive heart failure, that the musculature of the heart is satisfactory and preferably that there is no valvular disease.

4. A detailed report is made concerning seven patients who were selected for sympathectomy. They are all alive, three months to two years following operation. Three were rendered absolutely free from anginal attacks immediately and have remained so. Three continued to have typical anginal attacks after the operation but were nevertheless considerably improved, in that it required a greater effort to bring them on. One was made neither better nor worse. Of these latter four, three have since become practically free from attacks as a result of medical care. An eighth patient died on the day of the operation. It had been decided after careful study that he was a distinctly unfavorable case to be treated surgically, but because he was growing worse and life was becoming unbearable despite a ten weeks' course

of medical care, including antisyphilitic treatment, the operation was performed although we were fully aware of its dangers.

5. It is urged that cases be reported in detail so that one may judge as to the type of patient operated upon.

6. In general it is felt that the operative measures for angina pectoris if carried out on properly selected patients are a distinct addition to our means of therapy.

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(*For discussion see page* 118.)

THE ECONOMIC PHASES OF CARDIAC DISEASE*

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TO THE physician, concerned with the care of his patients, the social and economic effects of cardiac disease may seem of minor importance; to the patient and the immediate family, particularly if either parent be the patient, the physical suffering may be even less distressing than the disturbance of family life and the straitened financial circumstance, perhaps the destitution, which so often accompany an illness of long duration. This paper is presented with the hope of promoting a more lively appreciation of these social and economic aspects of cardiac disease.

The statistics herein presented have been obtained from the charts of patients with heart disease who have been under treatment in the Cook County Hospital or have attended the Cardiac Clinic at the Dispensary of the Northwestern University Medical School. For much of the material, I am indebted to Miss Zoe Harpster of the Social Service Department at Northwestern University and to Miss Jean E. Wilson of the Social Service Department at Cook County Hospital.

The charts of 200 recent patients at the County Hospital were studied. In 107 of these the heart disease was of the infective type, either rheumatic or syphilitic. Of this group 91 or 85 per cent were under fifty years of age. Seventy-one or 66 per cent were between the ages of twenty-one and fifty. Of those with some form of degenerative disease, 25 or 27 per cent were within the age limits of twenty-one and fifty. Thus, in the entire group of 200, ninety-six, almost one-half of the total, were men and women in their prime as years go. Actually, most of them were totally disabled without hope of restoration to normal conditions of life, condemned to the acceptance of public or private charity.

Of the entire group of 200 patients, eight had been patients in other institutions, twenty-two had already been in the County Hospital more than once. In this latter group the number of admissions varied from two to nine. Forty-six of the patients whose charts were studied had been readmitted to the hospital within six weeks of a prior discharge. Such a percentage of early readmissions is probably not maintained throughout the year. This study covered the months of January, February and March at which time the hospital is often overcrowded and constant vigilance is necessary to provide room for the many seriously sick people who seek admission. It seems fair to assume that about 20 per

*Read before the American Heart Association, Atlantic City, May, 1925.

cent of the patients with heart disease discharged from this public hospital will return for hospital care within six weeks.

These early readmissions, implying economic and human waste, are largely due to two causes: (1), those patients who consent to accept the services of a large charity hospital are likely to be both physically and financially exhausted, needing a long period for recuperation and utterly unfit to provide for themselves unless their physical condition is decidedly improved; (2), in general, neither public nor private hospitals have yet realized the necessity of prolonged rest for the patient with heart disease if he is to have the chance to attain a degree of health which will enable him again to become really self-supporting. The urgent need for convalescent institutions for cardiac patients needs no emphasis in the presence of these figures.

The charts studied were taken as they stood in the files marked Chronic Myocarditis, Organic Heart Disease and Acute Endocarditis. In 1923 there were in these three groups 1,236 cases. On the basis of percentages cited, some 700 of these patients were under fifty years of age. In the course of a single year about 250 individuals with chronic heart disease will be readmitted to the wards of the hospital, within six weeks of a prior discharge. Many of the patients will have three or more admissions. In the groups just mentioned the annual report for 1923 has no record of any patient being discharged as "cured." Seven hundred and six were discharged as "improved"; 205 as "unimproved." There were 325 deaths. The total admissions for all forms of heart disease including aneurysm of the aorta were 1,324. There were 349 deaths. As the cause of death cardiac disease was only exceeded by pulmonary tuberculosis and pneumonia.

The social service records of 18 patients were reviewed as illustrative of the effects upon the individual and his family. One group of ten consisted of patients between the ages of thirty-five and forty-five, nine of whom were married men, one a widow. In the families represented, there were twenty-nine children, all of whom were under eighteen years of age. Eight of these ten families are receiving outside help. In three instances this help comes from the United Charities or the Catholic Charities, the County Agent and the Mother's Pension Fund. One or more of these same agencies is giving aid to the other five families. The second group was made up of single men, whose ages ranged from twenty-five to sixty-two. Three of these men are now living upon the bounty of friends, two are inmates of the County Poor Farm, two are subsisting upon public charity and one, a foundry worker by trade, is earning a living as a dishwasher in a restaurant. Fortunately such dependence is not universal among the families represented in the wards of the County Hospital, but one familiar with the constituency of the hospital knows that these records of poverty due to cardiac disease picture actual conditions in hundreds of families in Chicago.

The Cardiac Clinic at Northwestern University Medical School was established two years ago. This clinic is open once a week. Many patients with cardiac disease are admitted to the general medical clinic, which is open daily, and are not transferred to the Cardiac Clinic. Hence the figures from the latter cover only a part of the patients with heart disease who have been treated at the dispensary. Since its inception, the Cardiac Clinic has admitted 249 patients of whom 169 had decompensated heart disease. Ninety-three had heart disease of the infective type, of whom 78, or 84 per cent were under fifty years of age. Of the 76 patients with other types of disease, 29, or 38 per cent were under fifty. Seventy-four, or 43 per cent of these patients with decompensated hearts had been, once or several times, patients in other institutions. This large proportion is due to the custom of referring from charity hospitals patients to the cardiac clinics connected with the various schools.

Of 169 families represented, 57 have been recipients of aid from the United Charities or the Catholic Charities. Approximately accurate figures were obtained as to the incomes of 102 patients. These figures are based upon the statements of the patients as to average income before the onset of symptoms and the approximate average income since disability began. The average income prior to disability was $92 per month; after disability the average monthly income was $39. For this group with partial disability the average loss of wages was $5,406 per month which amounts to a trifle less than $65,000 annually. The average duration of partial disability as determined for the whole group was 5½ years. To avoid exaggeration we may accept one-half of this as the average of partial disability and the total loss of wages to the patients in this small group amounts to about $170,000.

Most records of the patients in the group just described also contain information as to the duration of total disability. There were in all 72 charts in which the duration of total disability was stated. The average duration of such disability was 1½ years. Upon the basis of an average income of $1104, the loss in wages to these 72 people over a period of a year and a half would be about $120,000. Many of these patients were attending the medical dispensary before the Cardiac Clinic was opened and have been known to us for years. The period of disability as stated is not exaggerated.

Another phase of the economic loss resulting from cardiac disease is the gradual change in the economic position of many individuals. Not every patient with heart disease finds himself suddenly unfitted for his usual work. Often the skilled or experienced man will attempt to keep up the work for which he is fitted even under the handicap of partial disability with the hope that he will shortly be able to undertake his usual duties. Gradually it develops that the patient cannot meet the physical requirements of the occupation for which he was trained; eventually, the skilled

and well-paid laborer finds that his inability to work regularly and to maintain the pace of his healthy fellow-laborer is not satisfactory to his employer and he is compelled to seek work suited to his physical capacity with little or no regard for his equipment of skill and experience. In the aggregate, thousands of individuals find themselves slipping from the ranks of skilled laborers; more or less abruptly they are forced to the acceptance of work which, in the economic scale, is far below their capacity.

Of the patients seen at the Northwestern University Dispensary, 45 are stated to have had no trade. Among the others there are interesting illustrations of the statements made above. Eight men who had worked at common labor, of the harder but better paid sort, had been obliged to give up such work and accept occasional work such as porter or cleaning work. Two former chauffeurs made a living as watchmen, another as a dishwasher. One former special policeman and one painter were employed as watchmen. Two machinists had taken work as assistants or helpers. There was one instance each in which a brakeman, a moulder, a plasterer, a bricklayer, an ice-handler, a carpenter, and a barber, finding themselves unequal to their regular work, were working as helpers in their usual trades or doing occasional labor. Three men who called themselves building laborers and two blacksmiths were fit for no work except occasional labor of the lighter sort. One practical nurse could only undertake such work as promised to be easy. In five instances women who had done laundress or cleaning work at $4 a day were doing easy housework for less than half the former wage. In the entire group there are seven classified as students; some of these, since coming under observation have left school to begin remunerative work. All of these latter have been compelled to accept work at about half the wage common for young people of the same age. The cardiac disease, even though sufficiently compensated to permit of their undertaking remunerative work, has so interfered with their training, that from the economic standpoint, they are rated as worth about half as much as their healthy fellow-students. Not the least significant of these tabulations is one which shows that in the group are included twenty-two housewives who had formerly done their own housework; after the onset of the cardiac disease this work was done by the husband or by children with some help from the patients. The consequent disruption of normal home life needs no emphasis.

These figures become more impressive when we consider the earning capacity of the patients in the clinic. An average income of less than $1,200 a year for city dwellers marks them as belonging in the main to the poorest paid class of laborers. Of the 102 patients whose incomes are used as the basis of this discussion, 83 were men, 19 women. Of the men, 66 were employed in occupations classed as unskilled. Of the 19 women, 10 did laundress or cleaning work. If the economic loss caused by cardiac disease among a small group of persons who do the work for

which the community pays the least mounts to such figures as have been given, the results which might be obtained by a similar study of better paid persons would soon impress one as fabulous. If we were to use these basic income figures and multiply them by the numbers of cardiac patients annually receiving care at the County Hospital the total loss of wages alone would be startling. If three weeks (and this estimate is conservative) may be regarded as the average duration of each patient's stay in the hospital, 1,300 patients annually would have a total period of hospitalization of 3,900 weeks or 27,300 days. Estimating the cost of maintenance of each patient at the low figure of $2 a day, makes a total annual outlay for the care of patients with heart disease in this one hospital of $57,600. Some 65 patients under sixty years of age are sent each year from the County Hospital to the County Poor Farm as totally and permanently disabled by cardiac disease. The money expended for the maintenance of free beds in private hospitals and the amounts disbursed by various public and private agencies in Chicago to provide necessities of life for the patients and their families have not been estimated.

This brief and incomplete review covers only a few patients from two institutions and is almost entirely concerned with the poorest paid class of labor. If we were to multiply these figures by the number of institutions throughout the land where indigent cardiac patients are treated and by the number of public and private agencies extending aid to them, the tremendous economic waste directly due to chronic heart disease would be almost unbelievable. And such figures would not include the even greater number of better paid people who enter hospitals as private patients or spend all their days of disability at home. Neither have we touched upon the economic burden laid upon those who must support the sick, particularly the mothers or children who must assume support of families in so many instances. And the loss to society occasioned by the hampered lives of another generation, the inability of children properly to fit themselves for remunerative labor, often associated with loss of initiative and self-respect because of the constant dependence upon charity, is not to be stated in figures.

SUMMARY

About one-half of the patients with chronic heart disease with decompensation are of an age at which the earning capacity should be at its maximum and family responsibilities are likely to be most pressing. These individuals are afflicted with a disease which causes partial disability for years, and total disability extending, on the average, over a year and a half. In a single dispensary one-third of the families represented were dependent upon charity for their sustenance. Figures have been presented from two institutions which show that the economic loss, private and public, covering only a fraction of the patients with heart disease in one of our large cities must be estimated in hundreds of thousands of dollars annually.

(*For discussion see page* 117.)

THE STATUS OF THE HEART IN MYXEDEMA*

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VERY little concerning the status of the heart in cases of myxedema is recorded in the literature.[4, 8] An interesting article by Fahr, "Myxedema Heart" appeared recently, describing one case and referring to three others under observation. From these he concluded that definite objective signs and subjective symptoms of heart failure occurred which did not entirely respond to treatment by rest and digitalis, but were cured by thyroid medication. He believes that enormous dilatation of all chambers of the heart and negativity of the T-wave in Lead I of the electrocardiogram are characteristic of myxedema heart, and that the dilatation rapidly disappears and the T-wave becomes positive under thyroid medication. In a few cases there are notched and widened QRS complexes of delayed intraventricular conduction, which also disappear under thyroid treatment. Fahr also observed that the negative QRS complex in Lead III becomes positive under treatment.

CASES STUDIED

We have been greatly interested in myxedema, and as our attention had not been directed to some of the findings described by Fahr, we undertook a critical study of 162 cases of high grade myxedema, with special reference to the cardiovascular system.

Myxedema is a constitutional disease due to a decrease or absence of the secretion (thyroxin) of the thyroid gland as a result of its atrophy or removal, and characterized by a markedly decreased basal metabolic rate, a general myxedematous condition of the tissues, a slowed, impaired mental state, a typical facies, and other secondary manifestations.[1] All the cases studied conformed definitely to this type. Cases of postoperative myxedema were not included; thus we were enabled to eliminate possible residual cardiac damage from previous exophthalmic goiter or adenomatous goiter with hyperthyroidism.

AGE AND SEX

The greatest incidence in our series occurred in the fourth, fifth, and sixth decades, in which thirty-two, fifty-two, and thirty-eight cases, respectively were recorded (Table I). There were 128 females and

*From the Section on Cardiology, Mayo Clinic, Rochester, Minnesota.
Read before the American Heart Association, Atlantic City, N. J., May 26, 1925.

TABLE I

AGE INCIDENCE BY DECADES

	DECADES								
Number of cases	First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Total
	2	8	10	32	52	38	18	2	162

thirty-four males, a ratio of 5:1. This is in agreement with the sex ratio in other thyroid disorders.

CARDIOVASCULAR FINDINGS

In 148 patients (91 per cent) there were no subjective symptoms or objective findings indicative of organic cardiovascular disease. Eleven patients (7 per cent), however, presented unmistakable evidence of organic cardiovascular disease which was, in only one instance, appreciably influenced by the disappearance of myxedematous symptoms under thyroid treatment. Five patients had cardiac hypertrophy with varying degrees of myocardial insufficiency associated with hypertension; one patient presented the congestive failure type of cardiac disease associated with advanced cardiovascular renal disease, and another had the arteriosclerotic type of cardiac disease with angina pectoris. Three other patients complaining of exertion dyspnea associated with definite cardiac enlargement, in whom the type of lesion was indeterminate, showed no improvement in the cardiovascular condition under thyroid medication. These patients have been under intermittent observation for one, three, and four years, respectively. One patient, a man aged forty-eight, who complained of exertion dyspnea and bradycardia associated with attacks of extreme weakness, had moderate cardiac enlargement, the heart measuring 3.5 by 12.0 cm., and an electrocardiogram revealed broadening and notching of the QRS complexes in all leads. Some improvement was noted in the cardiac symptoms with the disappearance of the myxedema, and the QRS changes in the electrocardiogram disappeared. There was no diminution in the size of the heart, slight dyspnea still persisted, and subsequently the T-waves in Leads II and III of the electrocardiogram became negative, increasing the probability of associated degenerative myocardial changes. The incidence of organic cardiac disease in myxedema is not greater than that in any associated disease.

In three cases (2 per cent) we observed the development of cardiovascular disease after the myxedematous stage was passed. The first patient, a woman aged thirty-eight, was under observation for seven years, and during the last year and a half developed a malignant hypertension which recently caused her death. The second patient, a woman aged thirty-six, presented no evidence of cardiovascular disease, and radiological study did not reveal cardiac enlargement. After the first

year of thyroid treatment, rapid auricular fibrillation occurred with moderate cardiac dilatation. The basal metabolic rate at no time was elevated beyond the limits of normal. The third patient, a woman aged sixty-one, was under observation for four years. At the initial examination no cardiac enlargement was observed, and the blood pressure was normal, the systolic being 124 mm., and the diastolic 86. Three years later a well-established essential hypertension was noted.

PHYSIOLOGICAL CHANGES IN THE CIRCULATION

Interesting physiological changes affect the cardiovascular system in cases of myxedema, which are apparently chiefly influenced by the attendant reduction in the basal metabolic rate. These physiological alterations are best observed under basal conditions, as the stresses of ambulation may obscure the fundamental reactions owing to the adaptability of the cardiovascular mechanism even under the influence of metabolic sluggishness.

TABLE II

THE BLOOD PRESSURE, PULSE, AND BASAL METABOLIC RATE*

BEFORE TREATMENT						AFTER STABILIZATION FOLLOWING TREATMENT				
Basal metabolic rate	Cases	Blood pressure		Pulse pressure	Pulse rate	Basal metabolic rate	Blood pressure		Pulse pressure	Pulse rate
		Systolic	Diastolic				Systolic	Diastolic		
−10 to −19	18	111	74	37	69	+3	112	65	47	79
−20 to −29	45	113	75	38	65	+4	114	71	43	78
−30 to −39	67	108	73	35	61	+5	113	68	45	76
−40 to −44	12	109	74	35	59	+5	115	69	46	80
Total	142									
Average		110	74	36	63	+4	113	68	45	77

*Average of four or five readings in each case.

The average basal blood pressure and pulse rate readings of 142 cases grouped according to ranges of ten of the basal metabolic rate before and after stabilization by treatment are shown in Table II. The average systolic blood pressure in the group was 110 mm., the average diastolic 74; the average pulse pressure was 36 mm. and the average pulse rate 63. It is evident that the reduced pulse pressure occurs from a reduction in the systolic pressure associated with a drop in the pulse rate. After elevation of the basal metabolic rate and its stabilization under thyroid treatment the average basal metabolic rate was + 4 per cent, and the average blood pressure readings were: systolic 113 mm., diastolic 68, pulse pressure 45 mm., and pulse rate 77. The pulse pressure attains normal largely through a reduction in the diastolic pressure, while acceleration of the pulse rate occurs.

Boothby has shown that the circulation rate increases proportionately with the increased consumption of oxygen due to work. Although it has not been demonstrated experimentally, it is reasonable to assume that a decrease in the circulation rate accompanies a decrease in metabolism in myxedema, with corresponding change in blood pressure and pulse rate.

CHANGES IN BLOOD VOLUME

Blood volume determinations by the vital red method of Keith, Rowntree, and Geraghty were made in two cases. In one case in which the basal metabolic rate was −32 per cent, the plasma volume was 46.4 c.c. for each kilogram of body weight. The Palmer hemoglobin estimation was 88 per cent and the hematocrit showed the red cell volume to be 37 per cent. Three days after the intravenous administration of 5 mg. of thyroxin, the basal metabolic rate had risen to −7 per cent, and the comparative figures for the readings were: plasma volume 53.7 c.c. for each kilogram of body weight, the Palmer hemoglobin 82 per cent, and the red cell volume 32 per cent by the hematocrit.

In another case the figures were complicated by obesity. Comparative figures are of value, however, and the changes, although slight, show definite variations with the corresponding variations in metabolism.

DATE 1922	BASAL METABOLIC RATE, PER CENT	PALMER HEMOGLOBIN, PER CENT	HEMATOCRIT, PER CENT	PLASMA VOLUME, C.C. FOR EACH KILOGRAM
1-9	−30	86	44	32
1-13	−17	77	34	34
1-20	+ 6	73	35	35

These figures show a definite increase in the circulating blood plasma and a corresponding drop in hemoglobin which in all probability is a dilution phenomenon; this mobilization of body fluids into the general circulation was anticipated by H. S. Plummer.[8]

ELECTROCARDIOGRAPHY

In fifty-five cases (34 per cent) electrocardiographic examinations were made. The cases are presented in three groups: (1) those having tracings taken before treatment; (2) after treatment, and (3) both before and after treatment.

Group 1 (Thirty Cases).—The electrocardiograms in twenty of the cases (66 per cent), with records only before the institution of treatment, were normal, aside from the graphic evidence suggestive of ventricular preponderance. In the remaining ten cases (34 per cent) the tracings disclosed graphic abnormalities as follows: T-wave negativity in Lead I, one case; T-wave negativity in Leads I and II, three

cases; T-wave negativity in Leads II and III, two cases; T-wave negativity in all leads, three cases; and aberrant QRS complexes in all leads, one case. Five of these patients had independent associated organic cardiovascular disease.

Group 2 (Six Cases).—In four of the cases (66 per cent) in which electrocardiograms were taken only after the institution of thyroid treatment, the tracings were normal. In one case malignant hypertension developed after seven years of treatment and observation, and the tracing at this time showed T-wave negativity in Lead I. The other case disclosed auricular fibrillation one year after treatment.

Group 3 (Nineteen Cases).—In these cases electrocardiographic study was made before and after treatment, and many interesting transitions were revealed. In four cases the tracings were normal before treatment, as well as during the remainder of observation. In twelve cases changes occurred in the electrocardiograms following treatment. In four cases T-wave negativity in Lead I disappeared in an average of six weeks after the institution of thyroid medication; T-wave negativity in Leads I and II in two cases disappeared in an average of three and one-half months; T-wave negativity in Leads II and III in four cases disappeared in an average of six months, and T-wave negativity in all leads in one case disappeared in two weeks. In one case, delayed A-V conduction (0.24 second), not abolished by atropine, disappeared three months after treatment.

In twenty-eight cases of this series (54 per cent) the tracings were normal during the stage of high-grade myxedema; in twelve cases (23 per cent) the graphic abnormalities disappeared under the influence of thyroid medication, and in twelve cases (23 per cent) the studies were too incomplete to draw conclusions.

It is probable that an actual myxedematous change in the myocardium explains the electrocardiographic abnormalities that disappear with treatment. This concept is in accord with the other changes that occur in myxedema that are relieved by thyroid medication: namely, the disappearance of the myxedematous condition of the skin with consequent change in facies, the disappearance of mental retardation, the return of normal speech, the return of agility of movement, the return of normal speed of tendon reflexes, the disappearance of nerve deafness, and the improvement of vision.

CONCLUSIONS

In 162 cases of high-grade myxedema studied, none of heart failure and none of organic cardiovascular disease was found that could be justly attributed to the myxedema. There were numerous electrocardiographic abnormalities which disappeared under thyroid medication. The data presented do not justify the establishment of a cardiac syndrome characteristic of myxedema.

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(*For discussion see page* 123.)

POSTURAL HYPOTENSION

A Report of Three Cases*

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WE wish to report the clinical and pharmacological observations upon three patients whose blood pressure readings show extremely wide variations upon change of position of the body.

The complaint of each individual has been the occurrence of syncopal attacks after or during exertion or even after standing erect for some minutes. Other features in the three patients are a slow unchanging pulse rate, incapacity to perspire, a lowered basal metabolism and signs of slight and indefinite changes in the nervous system. Each of these patients felt much worse during the heat of summer.

The history of the first patient who came to our attention will be given in detail, the records of the two later patients will be summarized.

Case 1.—L. H., a white male of German birth, aged thirty-nine years, was admitted to the New York City Hospital on October 9, 1919. He complained of dizziness, attacks of syncope, and, in his own words, "terrible weakness."

Three years before his admission he had the first sudden attack of unconsciousness, two months later there was another attack, both attacks occurring without any cause of which he was aware. With succeeding recurring attacks he noticed that the syncope was caused by exertion and in this early part of his illness he also noticed profuse sweating and occasional slight swelling of the legs.

During the year previous to admission to the hospital the syncopal attacks became more frequent, the urine excretion, especially at night, was much increased in amount and in frequency, he lost sexual power, and, instead of the profuse sweating, he found he did not perspire under any conditions. His highest weight had been 155 pounds; in October, 1918, it was 145, and when admitted it was 119. This loss of weight may have been caused in part by insufficient nourishment due to lost earning power.

He had measles as a child, a badly infected hand when twenty-nine years old, vague aches and pains which never crippled any joint but had been called "rheumatism," and marked constipation for many years. He denied venereal disease, but admitted smoking and drinking to excess at times. He seemed to be fairly intelligent but said he had always done common laboring work.

The following notes upon his condition have been compiled from numerous examinations by members of the visiting and interne staff. Except for slightly increasing pallor and minor fluctuations in weight his condition does not differ from that on admission five years ago. He does not appear to be as old as thirty-nine years and lies in bed without any sign of distress. The skin looks pale but is smooth and is not pigmented except for three small patches of brownish pigmentation upon the thorax. His nutrition is poor, the muscles are well developed. The mucous membranes are pale, slightly bluish and there are no patches of pigmenta-

*From the Second Medical (Cornell) Division, Bellevue Hospital and the Department of Medicine, Cornell University Medical College.

tion. Beard, axillary and pubic hair are sparse but normally distributed. The eyeballs are deeply set (he says they have receded), pupils are oval but react promptly to light and accommodation, visual fields and fundi are normal. There are no enlarged lymphatic glands and the thyroid is not enlarged. Expansion of the thorax is fair and equal upon the two sides. The lungs are normal to auscultation and percussion. The heart is not enlarged, its action is slow and regular and there is a short systolic murmur at the apex which is probably functional. The abdomen is normal, the external genitalia normal. The left lower extremity is noticeably smaller than the right but the muscles in each leg function well and the reflexes are normal.

The blood pressure on admission, while he lay comfortably in bed, was 110/65 mm.* Four days later, his position not being noted, it was 80/40 mm. As he appeared to be well he was gotten out of bed. During the months that followed it was noted that he became easily exhausted, was often dizzy when standing and would relieve either condition by crouching in a chair and pressing the folded arms into the abdomen. He complained of constant dull headache, of spots before the eyes and four to six times each night would get up to pass large amounts of urine.

Nearly a year after admission he was made to exercise for the purpose of noting the effect upon respiration and pulse rate. Immediately upon sitting down there was no dyspnea and no increase in pulse rate but after a minute the head fell back, the pupils dilated, there were slight convulsive movements, pallor and unconsciousness, and the radial pulse could not be felt. In five minutes he recovered consciousness, in ten minutes the blood pressure was 60/40mm.

A fortnight later the effect of the position of the body upon the blood pressure was studied. It was found that when he lay quietly in bed the systolic and diastolic pressures were normal or nearly so, and that as he sat up, and then stood, both systolic and diastolic blood pressures fell to extremely low levels. The following reading, taken November 17, 1920, is a typical example of the reaction to change in position in this patient.

BLOOD PRESSURE

	SYSTOLIC	DIASTOLIC
Standing	40	28
Sitting	42	20
Supine	105	60

It was found too that elevation of the foot of the bed caused a further rise in blood pressure, 120/80 mm.

Repeatedly, when standing, systolic pressure as low as 35 mm. has been noted, and on several occasions the systolic pressure has been only 30 mm. of mercury, with the diastolic pressure indeterminable, the patient swaying with faintness. The attacks of faintness or syncope occur when he stands or exerts himself, are preceded by a death-like pallor and sometimes accompanied by slight convulsive movements of the arms and head. Allowed to lie down he recovers rapidly and without confusion and in five minutes is able to sit in a chair. Regardless of his position, and therefore of his blood pressure, the pulse rate is always slow, varying from 60 to 66, except when his head is lower than the trunk, in which position the pulse rate may rise slightly.

Usually, during an attack of syncope, the pulse becomes slower, retains its regularity but becomes weak or imperceptible at the wrist.

*This formula for expressing blood pressure has been used throughout the text, the first numeral denoting systolic pressure, the second, diastolic pressure.

From December 22, 1920, to January 7, 1921, he was sent to the Second Medical (Cornell) Division at Bellevue Hospital for further study. There the observations upon blood pressure and its variations upon change of position were confirmed. The electrocardiogram showed no abnormalities and basal metabolism was 79 per cent, 21 per cent below the average normal.

Upon return to City Hospital he was given epinephrin hypodermatically three times daily. Upon this medication he was fairly comfortable, being able to walk about the ward and even to climb a flight of stairs. It was found that his standing blood pressure fell as it did without epinephrin but not to so great a degree. On May 31, 1921, while receiving epinephrin, the blood pressure standing was 55/25 mm., supine it was 110/70.

In July, 1921, because of the low basal metabolism, he was given thyroxin and took 0.6 mg. of this drug daily until March, 1922, when he had an attack of pneumonia. During the administration of thyroxin blood pressure readings were generally higher than before but there was the same marked drop in the erect position and after exertion. The effect of thyroxin appeared gradually to wear off as may be seen from the following observations made during these months.

	Dec. 2, 1921		Dec. 9, 1921		Dec. 30, 1921		Jan. 23, 1922	
Blood press.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.
Sitting	106	64	94	50	71	52	85	45
Standing	94	54	78	50	68	48	55	40
After walking	76	40	74	44	48	40		

Neither epinephrin nor thyroxin was of any permanent or marked benefit so they have been discontinued.

A number of other procedures have been tried in the attempt to maintain the blood pressure at levels at which he would be comfortable but without notable success. For two months he was kept in bed. An abdominal binder pinned on as tightly as was compatible with comfort helped very slightly. An increased water intake, up to 120 ounces a day for ten days, did not benefit, neither did it harm him except to markedly increase the nocturnal polyuria. Digitalis did not help in the slightest degree. Atropin and pituitrin were of no benefit. He said he felt better when taking strychnin but there was no effect noted upon the blood pressure.

It was thought that the instability of blood pressure was the cause of the nocturnal polyuria, water being stored in the tissues during the day while he sat in a chair, while improvement of kidney function at night was due to the increased blood pressure when he lay down. This has been shown to be the case for both dye and water excretion. While sitting in a chair or occasionally walking about 6 mg. of phenolsulphonephthalein was excreted at the rate of 16 per cent in the first hour, 11 per cent in the second hour, a total of 27 per cent in two hours. In bed several days later but otherwise under the same conditions, the dye was excreted at the rate of 25 per cent in the first hour, 20 per cent in the second hour, a total of 45 per cent in the two hours.

The hourly notation of urine excretion shows even more strikingly the effect upon kidney activity of his day's general blood pressure level. With each day's observation he took a liter of water at the beginning of the test and his regular meals and fluids during the day. There was no fixation of specific gravity at any time. Phenolsulphonephthalein and urine output tests have been repeated a number of times with similar results. A typical urine output examination follows:

FEBRUARY 11, 1921 IN BED AMOUNT OF URINE	TIME	FEBRUARY 16, 1921 UP AMOUNT OF URINE
10 c.c.	8 A.M.	22 c.c.
145 c.c.	9 A.M.	50 c.c.
250 c.c.	10 A.M.	130 c.c.
205 c.c.	11 A.M.	150 c.c.
310 c.c.	Noon	60 c.c.
	2 P.M.	270 c.c.
305 c.c.	3 P.M.	
160 c.c.	5 P.M.	60 c.c.
105 c.c.	7 P.M.	30 c.c.
1490 c.c.	Total day	772 c.c.
300 c.c.	Night	1080 c.c.
1790 c.c.	Total	1852 c.c.
1006 to 1024	Specific gravity	1009 to 1020

Other observations are, a moderate and very gradually increasing anemia with normal leucocyte and differential counts, negative blood and spinal fluid Wassermann reactions, blood sugar which is well within normal limits or sometimes below normal, and blood urea nitrogen which is constantly at the upper limits of normal. The latter is not reduced by rest in bed. Roentgenogram of the sella turcica fails to show abnormality.*

CASE 2.—D. A., a male of fifty years of age was admitted to Cornell Clinic April 25, 1922, complaining of syncopal attacks, exhaustion and insomnia. The first attack of syncope occurred without warning three years before admission. During the two years previous to our first observation the attacks of faintness or unconsciousness appeared almost daily and in the morning rather than in the afternoon. He noticed them particularly during or after the exertion of bathing and dressing. Climbing stairs exhausts him so that, as he says, he is "short of breath, blind and dizzy." The failure to sweat causes so much discomfort that in summer he goes to bed covered with a wet sheet. There is nothing in the history to indicate a chronic degenerative disease or the probability of any chronic infection.

He appears to be younger than fifty years of age. Though quite small in stature, he is well proportioned, well muscled and well nourished. Both pupils are irregular in outline, the right is larger but both react promptly. The knee jerks are unequal, the right being greater, though this is not constant. Heart, lungs and abdominal organs all appear normal. There is noticeable incurvation of the finger nails and the hands are square with short thick fingers. There is no pigmentation of skin or mucous membranes. There are no abnormalities of growth of hair or texture of the skin. The pulse rate has been slow under all conditions.

His blood pressure shows similar but wider variations than that of the first patient. At times when he is supine it registers 165/100 mm., but when he is erect it drops at once to 55/30 mm., the pulse meanwhile maintaining the same rate. Other observations are negative blood and spinal fluid Wassermann reactions, blood urea nitrogen of 22 mg. per 100 c.c.; basal metabolism 18 per cent and 13 per cent below normal.

After several visits to Cornell Clinic he was referred to the Second Medical Division, Bellevue Hospital. There it was found that the blood pressure range was:

	SYSTOLIC	DIASTOLIC
Lying flat	158	108
Sitting	100	70
Standing	52	40

*Dr. E. P. Shelby, who alternated with one of us in visiting the New York City Hospital, gave many helpful suggestions in the care and investigation of Case 1.

The day urine, while he was up and about, was 330 c.c., the night urine 1527 c.c. Electrocardiogram shows no abnormality.

To determine the influence of mechanical support of the blood vessels of the lower extremities and of the abdomen, the legs were bandaged firmly from below the ankles to the groins while the patient was lying flat in bed. Later, a many-tailed abdominal binder was applied as snugly as possible with the patient again lying supine. Determinations of the blood pressure, pulse pressure and heart rate were made as shown in Table I.

TABLE I

SHOWING THE INFLUENCE OF BANDAGING THE LEGS AND THE APPLICATION OF A TIGHT ABDOMINAL BINDER

POSITION	TIME	S.B.P.*	D.B.P.	P.R.	
Before bandaging					
Horizontal	2.23	166	110	60	
	2.26	158	110	60	
	2.29	158	108	58	
Standing	2.31	60	42	58	
	2.32**	52	40	?	
Horizontal	2.35	172	118	62	
	2.38	164	118	62	
	2.46	158	108	62	
Legs bandaged					
Horizontal	2.55	166	112	62	
	2.58	166	110	64	
Standing	2.59	100	64	62	
	3.02	78	52	64	
	3.05	68	52	62	
	3.08	72	56	64	(Comfortable)
Horizontal	3.09	112	74	62	
	3.12	156	108	64	
	3.15	166	112	64	
	3.18	166	108	64	
Abdominal binder applied					
Horizontal	3.23	150	106	62	
	3.26	152	106	62	
Standing	3.27	98	64	62	
	3.30	66	52	64	
	3.33	76	58	64	
	3.36	78	55	64	
	3.56	68	48	64	

*S.B.P.—systolic blood pressure, D.B.P.—diastolic blood pressure, P.R.—pulse rate.
**At this point syncope developed and after five (about) beats of the pulse in the radial, at the rate of about one per second, the patient became pulseless and was lifted back into his bed. (Case 2.)

Following the application of the binder and the bandages the patient was up walking about the ward for several hours and remained quite comfortable. This procedure was repeated on several occasions with similar results.

CASE 3.—G. G., a white male aged sixty-seven years, was referred by Dr. H. J. Spencer and entered New York City Hospital, November 16, 1922. He complained of shortness of breath, pains in the region of the heart, numbness of the legs, forearms and hands, and attacks of syncope. Attacks of faintness had been present for many years but recently have been more severe and more frequent. For seven years past he has been unable to induce sweating even in a Turkish bath. He has an occasional cough, is short of breath when climbing stairs, the ankles swell at times and he must rise often at night to void.

He is an obese, well-developed, mentally active and emotional individual. The pupils are unequal but react to light and accommodation. The eyeballs are prom-

inent. The lips are slightly bluish. The thorax is of emphysematous shape but, except for weakness of the heart sounds, no abnormality could be found in heart, lungs or abdomen. The knee jerks are hyperactive and the Babinski reflex is present in each foot. The skin is dry and scaly but there is no pigmentation, except that of a wart on the face, and no pigmentation of the mucous membranes.

The blood pressure shows the same type of reaction as in the preceding patients but the variation is not so marked:

	SYSTOLIC	DIASTOLIC
Supine	84	60
Sitting	80	50
Standing	45	25

The pulse rate averages 65 per minute but rises occasionally to 80. The Wassermann reaction is negative, the blood urea nitrogen 23 mg., the blood sugar 110 mg. Electrocardiogram is normal.

Phenolsulphonephthalein excretion amounted to 50 per cent in two hours when in bed; when up and about to 35 per cent in two hours.

The urine excretion was as follows:

NOVEMBER 23, 1922 IN BED AMOUNT OF URINE	TIME	NOVEMBER 22, 1922 UP AND ABOUT AMOUNT OF URINE
120 c.c.	8 A.M.	0 c.c.
60 c.c.	9 A.M.	30 c.c.
50 c.c.	10 A.M.	0 c.c.
80 c.c.	11 A.M.	30 c.c.
65 c.c.	Noon	30 c.c.
120 c.c.	3 P.M.	25 c.c.
120 c.c.	5 P.M.	55 c.c.
280 c.c.	7 P.M.	225 c.c.
895 c.c.	Total day	395 c.c.
960 c.c.	Night	1020 c.c.
1855 c.c.	Total	1415 c.c.

The behavior of the blood pressures and the heart rate was so extraordinary in these three patients that we determined to carry out a series of investigations in the hope of throwing some light on the reason for the unusual responses. We present the protocol of a typical group of observations.*

THE EFFECT OF CHANGES IN POSTURE WITHOUT MUSCULAR EFFORT

CASE 2.—In order to study the reactions in as uncomplicated a manner as possible the patient was placed supine upon an operating table the top of which could be tilted as a whole with either the head or the foot downward. In these positions the top of the table could be placed at an angle of about 40 degrees from the horizontal, and the change could be effected within a few seconds. The patient was secured firmly between the foot plate of the table and two shoulder irons to avoid sliding

*On June 30, 1925, the three patients were followed up.

The patient reported as Case 1 is still at the City Hospital, has gained weight and appears to be stronger. There is no change in the anemia. His blood pressure is, standing 56/28, sitting 96/46, supine 118/72.

Patient reported as Case 2 died suddenly during the prolonged hot weather of early June. He had been under other care and is said to have improved slightly and to have recently perspired under the arms. Necropsy was not done.

The third patient reports by letter that his condition is unchanged.

when tilted. A manometer was kept in place on one arm for blood pressure readings. These were made by one of us while the other took simultaneous counts of the pulse rate and recorded the data with the precise times at which the determinations were made. Table II shows the results of such an experiment.

TABLE II

SHOWING THE INFLUENCE OF POSTURE WITHOUT MUSCULAR EFFORT*

(CASE 2)

POSTURE	TIME	S.B.P.	D.B.P.	P.R.
Horizontal	4.10	146	102	60
	4.13	153	106	58
	4.16	156	108	58
	4.19	156	106	56
**Foot down, at angle of 40° from horizontal	4.23	90	78	52
	4.26	90	78	54
	4.29	90	78	54
Returned to horizontal	4.32	140	110	54
	4.35	160	110	54
	4.38	158	108	54
**Head down, angle of 40°	4.40	172	116	54
	4.43	182	122	60
	4.46	180	122	60
Returned to horizontal	4.47½	164	118	56
	4.50½	158	108	56

*The patient was placed on an operating table, and fastened firmly between the foot rest and a pair of shoulder irons. Changes of position were effected by tilting the table, thus eliminating all physical effort on the part of the patient. S.B.P., systolic blood pressure; D.B.P., diastolic blood pressure; P.R., pulse rate.

**Here and throughout the discussion the terms "Foot down" and "Head down" are used to mean that the entire body, lying flat on the table, was tilted so that the patient lay at an angle of about 40 degrees from the horizontal with the foot end down and the head end up, or vice versa.

The effects of epinephrin, atropin and pilocarpin were then studied under the same or analogous conditions, and in each series of observations the patient was kept in each position until the readings became essentially stationary. Further, each test was preceded by a period of maintenance in the horizontal position until fixed readings were secured. The results of these pharmacological tests are summarized in Table III.

The dose of epinephrin was injected intramuscularly, the solution employed being freshly prepared to avoid the possibility of its having become weak or inert. The solution was also tested upon each patient by subcutaneous injection with ensuing blanching of the skin. Patient 1 received atropin subcutaneously, while it was injected intramuscularly in the others. No difference was noted. It is possible that the dose of atropin employed was too small, but it is the one commonly found to cause marked depression or paralysis of the cardiac vagus endings in most patients. Further, we noted dryness of the mouth and flushing of the skin in two of the patients. In the third, stimulation of the vagus by forced breathing and by direct pressure in the neck were without influence on the heart rate after the administration of atropin.

The administration of pilocarpin was followed by very profuse sweating in the second patient, and by marked sweating in the third. Salivation was present in both.

TABLE III

SHOWING THE SYSTOLIC, DIASTOLIC AND PULSE PRESSURES AND THE PULSE RATE FOR EACH OF THE THREE POSITIONS, AND BEFORE AND AFTER THE ADMINISTRATION OF EPINEPHRIN, ATROPIN AND PILOCARPIN

DRUG	HORIZONTAL				HEAD DOWN				FOOT DOWN			
	*S.B.P.	D.B.P.	P.P.	P.R.	S.B.P.	D.B.P.	P.P.	P.R.	S.B.P.	D.B.P.	P.P.	P.R.
Case 1												
None	108	70	38	67								
Epinephrin 0.6 mg.	140	62	78	124	132	90	42	73	92	50	42	62
None	106	72	34	62	154	68	86	148	108	50	58	108
Atropin 2.5 mg.	112	74	38	62	134	88	46	68	52	38	14	60
Case 2												
None	156	106	50	56								
Epinephrin 0.5 mg.	186	106	80	108	180	122	58	60	90	78	12	54
None	110	78	32	58	196	118	78	124	170	104	66	94
Atropin 2.5 mg.	120	82	38	58								
None	154	112	42	60								
Pilocarpin 6. mg.	80	62	18	58	150	108	42	64	58	46	12	58
Case 3												
None	110	65	45	68								
Epinephrin 1 mg.	122	65	57	76	118	70	48	70	92	60	32	68
None	108	68	40	68	160	76	84	98	130	68	62	88
Atropin 2.5 mg.	110	66	44	76								
None	94	66	28	64	134	88	46	78				
Pilocarpin 6. mg.	86	56	30	66	114	70	44	68	86	60	26	64
							Standing		50	34	16	68

NOTE: Where several consecutive readings at intervals of three minutes showed fluctuations of less than 5 mm. of mercury, we have averaged the figures to give a more accurate summary.

*S.B.P.—systolic blood pressure, D.B.P.—diastolic blood pressure, P.P.—pulse pressure, P.R.—pulse rate.

DISCUSSION

Hypotension is placed by most authors at and below 110 mm. systolic; Nicholson says below 100. Roberts[1] finds the lowest pressures in secondary anemia, pellagra, somasthenia, the neuroses and in pulmonary tuberculosis.

On the other hand Addis[2] found among 300 *normal* individuals two who had systolic pressures of 81 to 90 and 22 who had 91 to 100.

The lowest blood pressure figures we have found recorded are those given in Cannon's "Traumatic Shock." In six of 93 cases the systolic pressure was from 41 to 50.

The effect of changes in body position has been studied by several (Addis and M. A. Mortensen,[3] E. C. Schneider and Truesdell,[4] M. M. Ellis[5]). In general, for both men and women, the blood pressure response upon assuming the erect from a supine position is a slight drop in systolic pressure, a slight rise in diastolic pressure and a rise in pulse rate; the pulse pressure, of course, falling. In our cases the response in blood pressure to change from the horizontal to the vertical position of the body is always a marked drop in systolic and diastolic pressures and a variable change in the pulse pressure. The pulse rate does not change significantly but tends to fall slightly with lessened blood pressure.

In a search of the literature we have been unable to find any note of such wide fluctuations in blood pressure upon change of position of the body, nor of a condition similar to that noted in these patients. The three cases are similar in almost every detail. They all show the same sort of reaction to changes in position. All exhibit the effect of the generally lowered blood pressure during the day by lessened kidney activity. Each patient complains of absence of sweating. Each has slow heart action which is essentially unchanged by postural variations in the blood pressure level. Each exhibits similar reactions to atropin and epinephrin and Cases 2 and 3 show similar reactions to pilocarpin. They all have slight anemia, indefinite and slight changes in the nervous system, a lowered basal metabolism and blood urea nitrogen which is at the upper limits of the normal.

The chief points to be explained in our cases are the persistently slow heart rate and the remarkable behavior of the blood pressure.

Disease of the suprarenals was first thought of to account for the low blood pressure and the asthenia in these individuals. But we are convinced that this is not the explanation. Addison's disease is eliminated by the absence of all of its typical features, and by the fact that the condition did not progress during the several years over which these cases have been observed. The ill-defined syndrome known as hypoadrenia is of toxic origin and runs an acute course with early death or complete recovery, hence it does not in any way apply to

our cases. Similarly hypochromaffinism is to be excluded on account of the absence of evidences of congenital inferiority and the total lack of characteristic symptoms.

Persistent slow heart action may be due to a variety of conditions. Partial or complete heart-block usually causes more marked slowing than was present in these cases; complete block was ruled out by electrocardiographic records in all of the cases, and partial block by electrocardiograms and by the administration of atropin. There was no evidence in any of the cases that the slowed heart rate might have been due to such increased vagus activity as may arise from nasal, ocular or intestinal reflexes, increased intracranial pressure, gastric ulcer or cancer, uremia, or the presence of an excess of bile pigments in the blood. Further, the administration of atropin did not increase the heart rate, which should have been the case had the slowing been due to heightened vagal activity.

Ordinary syncopal attacks usually are due to transitory vagus stimulation from emotional or other temporary reflexes, and are not, as in these patients, dependent solely upon the effort to maintain the erect position. The only other common cause of recurring syncope is found in the temporary cerebral anemia associated with transitory disturbances of the cardiac rhythm. Although we made repeated careful observations during many attacks of fainting we never observed any appreciable alteration in heart rate, the regular rhythm was invariably maintained and electrocardiograms were normal. These cases, therefore, cannot be accounted for by any of the usual conditions which lead to abnormally low blood pressure or to repeated attacks of syncope.

The absence of sweating, which was conspicuous in all of the patients, cannot be explained on the basis of the low blood pressure since the pressure was within normal limits or even above normal with the patients lying in bed, and sweating was never observed at such times. It seemed possible that it was due to some disturbance in the sweat glands themselves or to a defect in their sympathetic innervation. The administration of pilocarpin, however, showed the glands to be capable of normal activity and that the sympathetic secretory endings were responsive to stimulation. The phenomenon of anhidrosis, therefore, remains unexplained, unless it be due to a greatly lowered state of activity on the part of either the sweat glands or their secretory nervous mechanism.

Diminution of normal sympathetic tone was suggested by the absence of cardiac acceleration following vagal depression by atropin and by failure of the heart rate to rise in response to sharp and very great lowering of the blood pressure when the erect position was assumed. The accelerator mechanism, however, was responsive to the

powerful sympathetic stimulant action of epinephrin. The rise in heart rate was very marked in the first and second patients, amounting to an increase of from 74 to 106 per cent of the original rate before epinephrin. These changes are shown in Table IV which is based on the figures given in Table III. The rise in patient No. 3 was much smaller. It is remarkable that in each of the three patients the greatest rise in the heart rate occurred when the head was lowered, the position in which the systolic pressures were highest. High systolic pressure usually results in cardiac slowing through stimulation of the vagus center. The observed absence of such stimulation suggests the impairment of vagus control.

TABLE IV

SHOWING THE CHANGE IN THE BLOOD PRESSURES, PULSE PRESSURE AND HEART RATE FOLLOWING EPINEPHRIN, CALCULATED IN TERMS OF PER CENT OF THE CORRESPONDING FIGURES BEFORE EPINEPHRIN

	HORIZONTAL	HEAD DOWN	FOOT DOWN
Case 1	per cent*	per cent	per cent
Systolic	+30	+16	+17
Diastolic	−11	−24	0
Pulse pressure	+105	+105	+38
Heart rate	+84	+102	+74
Case 2			
Systolic	+19	+ 9	+88
Diastolic	0	−13	+33
Pulse pressure	+60	+34	+450
Heart rate	+92	+106	+74
Case 3			
Systolic	+10	+35	+41
Diastolic	0	+ 8	+13
Pulse pressure	+27	+75	+93
Heart rate	+12	+40	+30

*The sign + indicates rise, - indicates fall, 0 indicates no change.

Epinephrin invariably raised the systolic pressure in these cases, and in all three positions studied; the increase varying between 9 and 88 per cent of the pressure before its administration. The effect on the diastolic pressure, however, was variable. With the patient horizontal there was no change in two and a fall of 11 per cent in one. When the head was down there was a fall in two and a small rise in one; while when the foot was down the diastolic pressure was raised by epinephrin in two and unchanged in the third. In six of the nine readings the diastolic pressure remained unchanged, or was reduced by epinephrin. The pulse pressure, like the systolic, was invariably raised, and usually to a very pronounced degree. The smallest rise amounted to 27 per cent, the largest to 450 per cent, and three of the determinations showed increases of 93 to 105 per cent. The percentage changes are shown in Table IV.

The mechanisms controlling the blood pressures in man are too complex to permit the successful analysis of the influences of epineph-

rin upon each factor separately. The factors of outstanding importance in these cases, however, are the observed changes in the heart rate, sympathetic augmentor stimulation and the question of stimulation of the sympathetic vasomotor endings. It is a well-established fact that epinephrin stimulates both the constrictor and the dilator endings, although the vasoconstriction normally predominates so greatly over the dilator influence that the effects of the latter are not observed in man until the constrictor action has passed off.

Analysis of the data supplied in Tables III and IV seems to show that epinephrin produced little or no vasoconstriction. This is indicated most clearly by the tendency of the diastolic pressure to remain unchanged or to fall. If the peripheral vessels were constricted some rise in diastolic pressure would be expected to follow unless antagonistic factors overcame the effects of constriction. While we cannot know all of these antagonistic factors, the most important and most easily observed factor of minute volume output of the heart can be surmised on the basis of changes in heart rate. The heart rate, however, was always increased by epinephrin, and, except in one instance in Case 3, to a degree which must be supposed to have effectively raised the volume output of the heart. If this assumption be correct it tends to confirm the evidence that but little if any vasoconstriction followed epinephrin. Epinephrin stimulates the augmentor endings of the sympathetic in the heart, and while this action cannot be proved to have occurred in our cases, it may be assumed to have taken place because the accelerator and augmentor responses always occur together. By thus increasing the force and completeness of ventricular systole the systolic blood pressure would be raised, especially when the heart rate is also increased. These two effects of epinephrin would explain fully the observed elevation in the systolic pressures in these cases in the absence of demonstrable vasoconstriction.

These deductions are supported by the evidence presented in Table V, in which the influence of posture on the blood pressures is calculated in terms of percentage change from the corresponding figures for the horizontal position. Reference to the figures for Case 1 shows the absence of vasoconstriction. The figures for the two other cases suggest slight constriction. In neither of these, however, is the occurrence of vasoconstriction proved, and the recorded blood pressure changes are explicable on the basis of combined augmentor and accelerator stimulation.

In fact, the tendency of diastolic pressure to fall in the horizontal and head-down positions after epinephrin (Tables III and IV) might be interpreted as evidence of some peripheral vasodilation, or at least of some diminished vascular tone. Either of these occurrences might be accounted for on the theory that the vasodilator endings in these cases are relatively hyperactive, or are hypersensitive to the

TABLE V

SHOWING THE CHANGES IN BLOOD PRESSURES, PULSE PRESSURE AND HEART RATE PRODUCED BY CHANGE IN POSTURE, BOTH BEFORE AND AFTER ADMINISTRATION OF EPINEPHRIN. THE CHANGES ARE CALCULATED IN TERMS OF PERCENTAGE OF THE CORRESPONDING READINGS IN THE HORIZONTAL POSITION

	HEAD DOWN		FOOT DOWN	
	Before epinephrin per cent*	After epinephrin per cent	Before epinephrin per cent	After epinephrin per cent
Case 1				
Systolic	+22	+10	−15	−23
Diastolic	+28	+10	−30	−20
Pulse pressure	+11	+10	+11	−26
Heart rate	+ 9	+19	− 7	−13
Case 2				
Systolic	+15	+ 5	−43	− 9
Diastolic	+15	+11	−26	− 2
Pulse pressure	+16	− 2	−76	−17
Heart rate	+ 7	+15	− 4	−13
Case 3				
Systolic	+ 7	+28	−18	+ 8
Diastolic	+ 8	+17	− 8	+ 5
Pulse pressure	+ 7	+47	−29	+ 9
Heart rate	+ 3	+29	0	+16

*The sign + indicates rise, - indicates fall and 0 indicates no change.

stimulant action of epinephrin. If this be the fact it indicates the presence of definite abnormality on the part of the sympathetic vasomotor endings. This suggestion is in close agreement with facts previously discussed.

Finally, it must be emphasized that the administration of epinephrin did not alter the direction of the changes in the blood pressures in response to postural change except in Case 3 when placed in the foot-down position. The differences observed before and after epinephrin are merely quantitative, and even these are not large. In other words, the nature of the blood pressure responses to the influence of gravity was unaltered by epinephrin in spite of the production of some increase of systolic blood pressure and more or less pronounced elevation of the heart rate.

SUMMARY

The one feature of outstanding interest and importance common to these three patients is the extraordinary dependence of the systolic and diastolic blood pressures upon the influence of gravity, as exerted through alterations in the positions of the body from the horizontal. The rise of blood pressures in the head-down position, and their fall in the foot-down or the erect position, occur almost immediately. The reactions are those which would be expected if the whole peripheral vascular bed were always wide open, inelastic, and capable of accommodating the major proportion of the entire blood

volume of the body. This is the only definite conclusion to which our investigations have led. The cause or causes of this remarkable absence of normal vasomotor control seem to us to be purely speculative. We wish, therefore, in offering the following suggestions as to possible causative factors to present them as hypotheses, not as conclusions.

1. There is in these three cases, an almost total loss of peripheral vascular tone, and a loss of the normal mechanism by which blood pressure is maintained in the different positions of the body.

2. There seems to be some extensive and peculiar disturbance in the functional activity of the vegetative nervous system.

3. The heart rate is uniformly slow and is essentially unaltered by the large changes in the blood pressures which follow change in position of the body.

4. There is evidence also for the belief that the sympathetic accelerator control of the heart is impaired. Atropin does not accelerate the heart rate, and pronounced fall in blood pressure causes no compensatory rise in rate.

5. The responsiveness of the vagus to pronounced elevation of blood pressure (posture and epinephrin) seems to be largely wanting.

6. Both the cardiac accelerator and the augmentor functions of the sympathetic can be stimulated by epinephrin, but such stimulation does not restore the capacity to maintain the blood pressure level in the face of the influence of gravity.

7. The responsiveness of the vasoconstrictor endings of the sympathetic to stimulation by epinephrin is much impaired, or entirely lost.

8. The inability to sweat, common to all three patients, is not due to defect in the sweat glands or to lack of their ability to respond to pharmacological stimulation of the sympathetic endings. Neither can it be attributed to the existence of abnormally low blood pressure.

9. Efforts to cure these patients, or to control their disorders, have been unavailing. These efforts have included the administration of thyroxin, epinephrin, dried suprarenal substance, mixed glands, strychnin, and digitalis, and the enforced consumption of sugar and of water.

10. Paralysis of the sympathetic vasoconstrictor endings seems to be the only adequate explanation of the blood pressure reactions observed in these three cases. It accounts for the absence of vasoconstriction following the injection of epinephrin. And it explains the total absence of the normal vasomotor control by which blood pressure is maintained at a nearly constant level in the face of changes in the position of the body in normal persons.

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THE CLASSIFICATION OF CARDIAC DIAGNOSIS, WITH ESPECIAL REFERENCE TO ETIOLOGY*

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A PAPER published by us in 1921[1] described a method of classification of cardiac diagnosis which had proved very practical and helpful in the analysis of patients seen in the Cardiac Clinic of the Massachusetts General Hospital. Other physicians agreed as to its worth in the clinical study of patients with heart disease. Since publication of the original paper certain advances have been made in the study of cardiac disease, and therefore, it has seemed advisable to revise the classification and to embody in this revision the most pertinent features of the recent contributions. In addition to our own experience, we are indebted to the writings of Mackenzie, Lewis, Cabot, St. Lawrence, Libman, and certain publications from the New York Heart Association. The original form published in 1921 was used by the New York Heart Association as a standard for diagnosis in their clinical charts. Previously at the Bellevue Hospital Cardiac Clinic in New York, Doctor Wyckoff had introduced a similar method of classification. Even though it has been used chiefly in cardiac clinics by specialists, it is believed that this classification is of equal value to the busy general practitioner. With the patient before him the diagnosis will be simplified if the physician will think in the terms to be discussed.

We still find, even in large medical centers, the continued use of such ambiguous terms as "mitral insufficiency," "myocarditis," and "intermittent heart." That these terms may have their place in diagnostic nomenclature is not denied, but when they are given as the complete diagnosis the analysis is obviously insufficient. Moreover to make a diagnosis such as "mitral stenosis," or "aortic insufficiency" or "cardiac hypertrophy," without other qualifying terms is also insufficient. Neither can we any longer be content with such functional diagnoses as "cardiac failure," "auricular fibrillation" and "heart block," with which as clinical entities many were recently content, following the revolution in internal medicine from the older dependence on anatomical pathology to the newer vogue of the interpretation of disease wholly according to functional disturbance or physiological

*From the Cardiac Clinic of the Massachusetts General Hospital and the Cardiac Clinic of the Des Moines Health Center.

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pathology. And finally in the light of our present knowledge of cardiac diagnosis one may say that even such etiological terms as "rheumatic heart disease," "syphilitic heart disease," or "arteriosclerotic heart disease" when intended to cover an entire diagnosis, though far more satisfactory than the above expressions, are still not complete in themselves.

What, then, does constitute a complete cardiac diagnosis? There are three main headings under each of which every patient with cardiac symptoms or signs should be classified. They are first, etiology; second, structural change; third, functional condition of the heart. In the past, as a rule, diagnosis has covered only structural or functional change; the functional ability of the heart—what the heart can do in maintaining the needs of the circulation—represents often, though not always, a more vital part of the diagnosis than does the anatomical change. Too little consideration has been given to the factors responsible for heart diseases. The determination of the etiology, besides allowing for much greater accuracy in diagnosis, prognosis and treatment, aids materially in the advance of the great nation-wide movement for the prevention of heart disease.

There are certain laboratory methods which may be needed in classifying the patient, such as the roentgen ray, the electrocardiograph, the Wassermann test, basal metabolic rate test, blood examination and urine examination. It should be said, however, that oftentimes clinical bedside examination alone is all that is necessary to arrive at a complete diagnosis.

In considering the different types of heart disease it will readily be understood that they are not all to be considered as definite and distinct disease entities, but rather that the manifestations of heart abnormalities are in some instances only localized evidence of general systemic disease. In the consideration of etiological types must be included not only the exciting cause—the etiological agent—such as bacterium, toxin or trauma, but also the predisposition of the patient, individual as well as hereditary, to the disease, and contributory factors which play their part, such as climate in rheumatic fever, and fatigue in effort syndrome. All these factors are here taken for granted as playing a greater or lesser rôle in the etiological types of heart disease. Also it must be realized that the separation between structural and functional conditions is not a wholly satisfactory one since physical or chemical changes in the myocardium, resulting in serious disturbance of function may produce structural change not yet apparent to us by our present methods of examination. Also at times it is difficult to determine the borderline between the etiological and the functional, as in the case of the mysterious condition "angina pectoris," and between the etiological and the structural, as in the case of coronary thrombosis. However, the separation of the three

groups of evidence of abnormality of the heart, etiological, structural, and functional, is in clinical medicine very reasonable and useful.

I. ETIOLOGY

1. Congenital heart disease.
2. "Rheumatic" type of heart disease, resulting from:
   - (1) Tonsillitis.
   - (2) Chorea.
   - (3) Rheumatic fever.
   - (4) Scarlet fever.*

   A. Active.
   B. Inactive.

This includes also patients with mitral stenosis and young people with aortic stenosis or regurgitation not the result of syphilis, even though a clear-cut history of any of these diseases of the rheumatic group cannot be obtained. This form of heart disease produces widespread damage to the heart, involving the myocardium, endocardium, the conduction system, and frequently the pericardium. It is a very common form in New England, causing at least 90 per cent of heart disease in young people, a form undoubtedly infectious in origin, and one offering great possibilities in the line of prevention. In some parts of the world this type of heart disease is rare. Every person who has had rheumatism or chorea is a "potential" cardiac patient.

3. Bacterial endocarditis, due to invasion by known organisms.
   - (1) Pneumococcus.
   - (2) Meningococcus.
   - (3) Staphylococcus aureus or albus.
   - (4) Streptococcus hemolyticus.
   - (5) Influenza bacillus.
   - (6) Gonococcus.
   - (7) Streptococcus viridans.

These kinds of bacterial endocarditis have been grouped sometimes in the past as "Malignant Endocarditis." They may be acute or subacute, lasting days, weeks or months, depending on the virulence of the organism. They are usually fatal, especially the more acute types which are apt to be terminal and often not recognized clinically. When very slow in course they have been called "endocarditis lenta," either malign or benign. The commonest cause of the so-called "subacute bacterial endocarditis" is the Streptococcus viridans, from which spontaneous recovery may take place. Streptococcus viridans endocarditis is a frequent terminal complication of "rheumatic" heart disease.

*It is possible that further investigation of heart disease resulting from scarlet fever may occasion a separate etiological type of "the scarlet fever heart."

4. Diphtheritic heart disease, apparently usually rapidly fatal.

5. Syphilitic heart disease and aortitis, varying in frequency considerably in different parts of the world and in different groups of society.

6. Other rare types of infectious heart disease, such as that due to the tubercle bacillus and to the echinococcus.

7. Thyroid heart disease.

A. Hyperthyroidism, resulting eventually in cardiac enlargement, often auricular fibrillation, and failure of the congestive type, which may be cleared up by eliminating the cause.

B. Hypothyroidism, attended by sluggish cardiac action. Fahr[2] states that in myxedema there are certain characteristic changes in the heart justifying the establishment of a "myxedema" type of heart disease. However, Willius and Haines[3] in a study of 162 cases of high grade myxedema state that "none of heart failure and none of organic cardiovascular disease was found that could be justly attributed to the myxedema. There were numerous electrocardiographic abnormalities which disappeared under thyroid medication. The data presented does not justify the establishment of a cardiac syndrome characteristic of myxedema." Be this as it may, there is sufficient evidence that in hypothyroidism the cardiac action is not perfectly normal.

8. Toxic heart conditions, as from metallic poisons and uremia, and possibly including the heart made irritable by tobacco, coffee and absorption from local infections such as chronic cholecystitis.

9. Hypertensive heart disease, the result either of essential "hypertension" or of nephritis, much more commonly the former. The expressions "cardiovascular renal disease" and "cardiorenal disease" are sometimes used; however, they are usually loosely employed and often given erroneously as a diagnosis in cases with arteriosclerotic or "rheumatic" heart disease with congestive failure and albuminuria. The cause of "essential" hypertension is unknown. The term used here—hypertensive—is, to be sure, only descriptive and not final, but it is still the best available at the present time to cover this common group of cardiac cases, characterized eventually by cardiac hypertrophy, with or without final congestive failure from fatigue, or complication by uremia or by coronary sclerosis.

10. Emphysema heart, with especial strain on the right ventricle.

11. Arterioselerotic heart disease, or the senile heart or cardiosclerosis, which is the commonest etiological type of all. There are three

chief types of arteriosclerotic heart disease: first, that in which heart failure of the anginal type is the first or prominent symptom; second, a form in which the congestive type of heart failure is the outstanding feature; and third, that in which auricular fibrillation dominates the clinical picture. Given a patient of the arteriosclerotic age who has one or more of these three syndromes, this form of heart disease will be found to be an etiological factor in most instances.

12. Angina pectoris, the cause of which is unknown though the condition itself is usually regarded as a symptom due to some disturbance of function. It is a distinct entity not necessarily associated with aortic or coronary sclerosis.

13. Coronary occlusion due to thrombosis or embolism, also a distinct entity, often associated with coronary sclerosis, and causing infarction.

14. The heart in severe anemia, usually with dilatation and various murmurs.

15. The nervous heart, or cardiac neurosis, or the irritable heart of soldiers, not strictly heart disease. This includes "effort syndrome" or "neurocirculatory asthenia," a condition which occurs frequently during convalescence from acute infectious diseases, operations and accidents. It is sometimes wrongly diagnosed heart disease; as for example "the influenza heart," or "the pneumonia heart." In a strict sense the nervous heart is not true heart disease, but it certainly causes "heart trouble."

16. Traumatic heart lesions—of valves, auricular or ventricular walls or aorta—the results of penetrating wounds, crushes, blows, or great strain.

17. Cardiac tumors, primary or secondary.

18. Other rare etiological types such as the "athlete's" heart, a doubtful entity, generally consisting of "effort syndrome," but rarely of slight cardiac hypertrophy from certain excessive athletic exercise such as professional ski racing or bicycle racing; the "beer heart"; and the heart in extreme obesity (an uncertain entity).

19. Unknown. If the cause of heart disease in a given case cannot be determined it should be so expressed for two reasons: first, in order to stimulate further study and longer observation of the patient, and second, to stimulate further investigation of heart disease generally.

The most common etiological types of actual heart disease are the arteriosclerotic, the hypertensive, the "rheumatic," and the syphilitic; but heart trouble due to the "nervous heart" is the commonest disturbance of all.

II. STRUCTURAL CHANGE

Probably this, the second portion of the diagnosis, will be the first to become clear to the examiner, since many structural changes are readily recognized. Oftentimes one cannot be clear as to the etiology until after determination of the type of valve impairment or of the size and shape of the heart.

1. Myocardial. It should be clearly understood that myocardial pathology, whether actual myocarditis (which is rare) or myocardial hypertrophy or atrophy (which are common), is included in this classification in the etiological type. Thus "rheumatic" heart disease implies involvement of the myocardium with the typical submiliary nodules of Aschoff; syphilitic heart disease implies possible invasion of the myocardium as well as of the aorta by spirochetes. Arteriosclerotic heart disease implies myocardial degeneration with fibrosis resulting; and hypertensive heart disease implies hypertrophy. When the etiological type of heart disease is stated the myocardial change associated with the type may be taken for granted although the degree of involvement varies greatly.

Myocardial infarction from coronary occlusion, if extensive, leading to cardiac aneurysm and perforation into the pericardium, is a structural change in the heart which is usually diagnosed at the necropsy table. There is clinical evidence of the condition, however, on occasion, in the presence of severe prolonged heart pain if the thrombosis is extensive. Arteriosclerosis is usually present.

2. Endocardial. The only portion of the endocardium giving evidence of damage clinically is the valvular endocardium. Therefore, clinical diagnosis of endocardial pathology has perforce to be limited to valve changes.

A. Mitral regurgitation, with or without clinical stenosis; this does not mean functional mitral regurgitation.
B. Mitral stenosis, with or without clinical regurgitation.
C. Tricuspid regurgitation, with or without clinical stenosis. This does not mean a functional tricuspid leak.
D. Tricuspid stenosis, with or without clinical regurgitation.
E. Aortic regurgitation, with or without stenosis.
F. Aortic stenosis, with or without clinically demonstrable regurgitation.
G. Pulmonic regurgitation.
H. Pulmonic stenosis.

3. Pericardial.

A. Acute fibrinous pericarditis.
B. Pericardial effusion: (a) serofibrinous; (b) purulent and (c) hydropericardium.

C. Adhesive pericarditis.

D. Pneumopericardium.

4. Cardiac size and position.

A. Enlargement, usually meaning both hypertrophy and dilatation, the exact amount of each being usually indeterminable.

B. Right or left ventricular preponderance; either the left or the right ventricle may be relatively more enlarged than the other. Roentgen ray evidence is often helpful, but electrocardiograms may be needed to demonstrate this condition by the finding of abnormal axis deviation.

C. Auricular enlargement; sometimes evident by roentgen ray or by electrocardiogram.

D. Dextrocardia.

The squat transversely placed heart of an obese patient and the vertical "narrow" or "ptosed" heart of the tall lean patient are in themselves unimportant. They are merely a feature of the given type of case.

5. Coronary vessels.

A. Sclerosis.

B. Embolism.

C. Thrombosis.

6. Cardiac chambers. Rare congenital abnormalities such as the heart with two auricles and one ventricle, two ventricles and one auricle, or one auricle and one ventricle.

7. Septal defects.

A. Interventricular foramen.

B. Foramen ovale.

8. Great vessels.

A. Aortic dilatation: (a) general; (b) saccular aneurysm.

B. Pulmonary artery dilatation.

C. Patent ductus arteriosus.

D. Coaretation of aorta.

E. Dextroposition of aorta.

F. Transposition of aorta and pulmonic artery (and other rare congenital defects).

III. FUNCTIONAL CONDITION

1. Heart failure.
   - A. Congestive type, as expressed by dyspnea, edema, cyanosis, engorgement of neck veins, cardiac dilatation, functional mitral and tricuspid regurgitation, and so forth. This, of course, may be of any degree.
   - B. Anginal type, already listed under etiology. It is expressed by paroxysmal heart pain.

An addition functional grouping such as that suggested by the New York Association of Cardiac Clinics is also very useful. It expresses directly the ability to work as follows.

- A. Able to carry on the patient's usual activities.
- B. Able to carry on slightly to moderately curtailed activity.
- C. Able to carry on only greatly diminished activity.
- D. Unable to carry on any activity (without distress).

2. Disordered heart action.
   - A. Sinus irregularities.
   - B. Premature contractions (extrasystoles); (a) auricular, (b) ventricular, and (c) junctional.
   - C. Paroxysmal tachycardia: (a) auricular, (b) ventricular, and (c) junctional.
   - D. Auricular flutter.
   - E. Auricular fibrillation.
   - F. Heart-block: (a) auriculoventricular; (b) intraventricular, including complete and partial bundle branch block and arborization block; and (c) sinoauricular, including auricular standstill.
   - G. Atrioventricular rhythm and ventricular escape.
   - H. Pulsus alternans.

ILLUSTRATIONS

To illustrate this classification and to show how satisfactory it proves to be in an analysis of a cardiac patient, the following diagnoses are added:

Case 1.—Rheumatic heart disease (inactive) with mitral stenosis, (right ventricular preponderance), auricular fibrillation and failure of the congestive type (able to carry on only greatly diminished activity).

Case 2.—Arteriosclerotic and hypertensive heart disease with cardiac enlargement, ventricular premature beats, pulsus alternans, and failure of the anginal type (unable to carry on any activity).

Case 3.—Cardiac enlargement and auricular flutter, of unknown cause (able to carry on slightly curtailed activity).

Case 4.—Syphilitic heart disease with aortitis, aneurysm of ascending aorta, aortic regurgitation (left ventricular preponderance, and normal rhythm) (able to carry on moderately diminished activity).

CONCLUSION

Every cardiac diagnosis should include three features: first, the cause, or etiology; second, structural change or changes; and third, the functional ability of the heart. All three are essential.

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(*For discussion see page* 118.)

THE CIRCULATION OF THE HEART VALVES

Notes on the Embolic Basis for Endocarditis*

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INTEREST in the etiological factors concerned in endocarditis has led to much discussion since 1852 when Luschka[1] first stated that there were vessels in the valves of the heart. He showed, by injection methods, that normal valves had small vessels to the line of closure and that there were a few vessels in the lower part of the chordae tendineae. In 1863[2] Luschka described vessels in the semilunar valves and suggested the relation of a richer vascularity of the aortic and mitral valves to endocarditis, more commonly noted in these valves. He indicated that the capillaries ended bluntly, which was probably due to imperfect injections. Joseph[3] opposed this theory as a basis for endocarditis and it was considered that the valves showing vascularity were diseased. Coen[4] in 1886 and Langer,[5] 1887, found no vessels in the normal semilunar valves and stated that the atrioventricular valves were only partially vascularized. Langer and subsequent writers considered that blood vessels in the valves were associated with smooth muscle fibers. They believed that only the basal third of the valves were vascularized. Tandler[6] believed that the vessels diminished with age, as a part of the developmental process, and were associated with the smooth muscle. He stated that there were small vessels in the atrioventricular valves and chordae tendineae, but that there were practically no vessels in the semilunar valves. Nussbaum[7] in 1912 demonstrated blood vessels in the membranous portion of the atrioventricular valves of child and adult. He was unable, however, to inject vessels in the chordae tendineae or semilunar valves.

Rosenow[8] in 1912 by the intravenous injection of streptococci, pneumococci and Staphylococcus albus in rabbits demonstrated clumps of bacteria in the valves of the heart, with associated hemorrhage into the structure of the valves. He reaffirmed the idea of embolic localization of bacteria as a cause of endocarditis.

MacCallum,[9] in 1916, by injection methods with india ink in the living heart, limited the blood vessels to the basal third of the atrioventricular valves. The pressure was probably not sufficient to insure complete injections.

The classical studies of Bayne-Jones[10] in 1917 furthered the conception of an embolic basis for the etiology of endocarditis. Injec-

*From the Department of Medicine, University of California Medical School.
Read before the American Heart Association, Atlantic City, N. J., May 26, 1925.

tions were made through the coronary arteries using a mass of carmine and gelatin, under 140-190 mm. Hg., with an air pressure apparatus. The temperature was kept at 45° C. and pressure was continued for thirty minutes. Then the specimen was plunged into ice water, after which it was fixed in formalin. After dehydration the valves were cleared with wintergreen. The results showed that, in the pig, the atrioventricular and semilunar valves and chordae tendineae were well supplied with vessels, and differed only in numbers from the human heart. He states that the blood supply of the atrioventricular valves comes from arterioles of the right and left coronaries

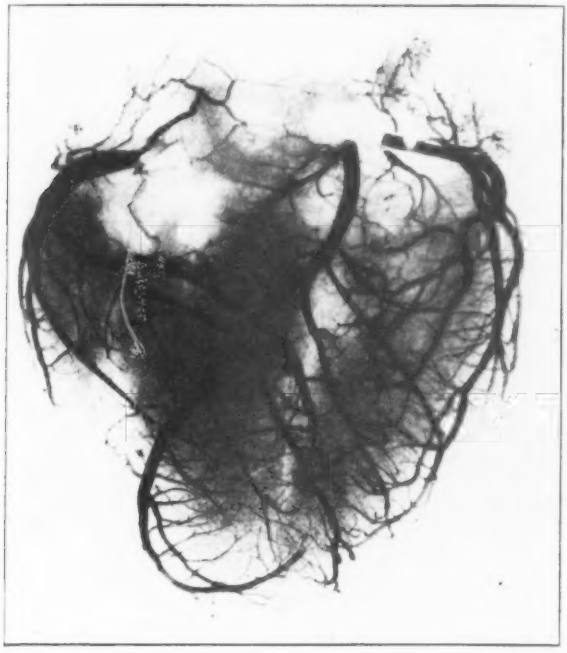

Fig. 1.—Bismuth-gelatin injection of normal coronary circulation of human heart. (Injection by Wm. B. Faulkner, M.D., and N. N. Epstein, M.D.)

as they pass through the annulus fibrosus at the A.-V. junction. Distinct anastomoses are shown and tufts of vessels occur at the lines of closure. No vessels were found, however, passing from the valves to the chordae tendineae and only occasional strands of small vessels were noted passing to the free margins of the valves. A distinct separation of arteries and veins was noted in the upper portions of the valves and constrictions of the arteries were observed at the points of branching. The chordae tendineae showed only slight vascularity, which was derived from the branches of the descending rami of the coronaries to the papillary muscles. From a subendothelial plexus here delicate vessels ran up to the chordae tendineae beneath the endo-

cardium or in the center of the tendons. The supply in the chordae tendineae of the pig was abundant.

Bayne-Jones described a hedge-like plexus in the semilunar valves occupying about one-half of the membranous portions. No vessels were shown in the thin portion of the valve cusps or in the noduli Aranti. He states that the blood supply of the semilunar valves is derived from two sources: (1) vas vasorum of the arteries; (2) vessels of the auricular endocardium. Only three successful injections of these valves were obtained. The drawings indicate that with better methods the

Fig. 2.—Corrosion preparation of coronary circulation (normal, human) after injection with celloidin mass. (Injection by Wm. B. Faulkner, M.D., and N. N. Epstein, M.D.)

entire valve leaflets could probably be injected. This excellent work lends further support to the view that endocarditis is embolic in origin, and gives an anatomical basis for this conception.

Vaquez[11] reviews the European literature on the experimental and clinical features of endocarditis.

"The infectious nature of endocarditis has been demonstrated by bacteriology and by experiment. Culture of the blood during life and the examination of the endocardial vegetations from the cadaver have revealed the presence of various bacteria, especially streptococci, pneumococci, gonococci and colon bacilli, more rarely tubercle bacilli. Sometimes there are combinations of bacteria.

"The first experimental researches were made by Gilbert and Lion who reproduced infectious endocarditis by injecting into the veins of an animal the bacteria taken from a subject suffering from this disease. Mannaberg and Vaillard obtained the same result with streptococci. Widal and Bezancon produced a mitral endocarditis by inoculating streptococci under the skin of a rabbit's ear. Michaelis and Blum, Bernard and Salomon claimed to have produced tuberculous endocarditis by injecting Koch's bacilli. Previous injury of the endocardium facilitates invasion by pathogenic bacteria, which explains why secondary endocarditis develops preferably in subjects already affected by an old valvular disease.

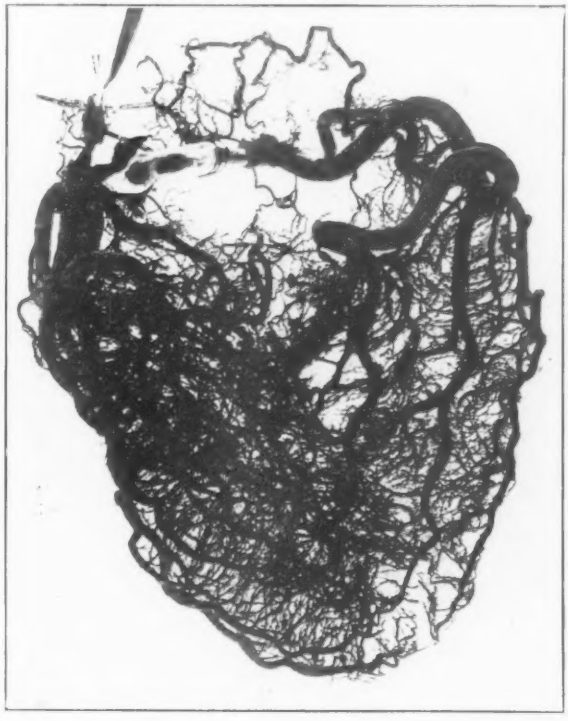

Fig. 3.—Corrosion preparation of human coronary circulation after injection with celloidin mass. Note tortuous coronary vessels. (Injection by Wm. B. Faulkner, M.D., and N. N. Epstein, M.D.)

"According to Klebs and Ortner, the bacteria are deposited directly on the surface of the endocardium. According to Köster, they are carried by the blood in the minute vessels of the valves to the neighborhood of their free border and there form thromboses which are the points of departure of the endocarditis. This latter explanation, advocated by Cornil and Babes and by Haushalter, is generally accepted.

"Any part of the endocardium may be attacked but especially the valves, either because of their prolonged contact with the pathogenic bacteria or more probably because of their great functional activity. The endocarditis usually involves the cavities containing oxygenated blood, those of the right heart in the embryo, of the left heart after birth.

PATHOLOGY

Pathology of Simple, Inflammatory or Plastic Endocarditis.—This corresponds to the type produced in rheumatic endocarditis. It is also called verrucous or exudative endocarditis. In the beginning, it is characterized by redness of the affected region which is more richly vascular than normal. This redness, which must be distinguished from postmortem staining, is particularly distinct if the valve-flaps are examined by transmitted light. Subsequently, the redness gives place to edematous swelling which tends to invade the free border of the valves. At this point, the endocardium, instead of being smooth and shining, is rough, or, rather, granular; then granulations appear, at first microscopic, gradually increasing to form vegetations of variable size.

"The vegetations consist of festoons of minute, rough nodules, translucent, of reddish or pale pink color, located a few millimeters from the free border of the valve. They are soft and friable, easily torn with the finger nail but they are none the less intimately united to the surface, from which they cannot be detached

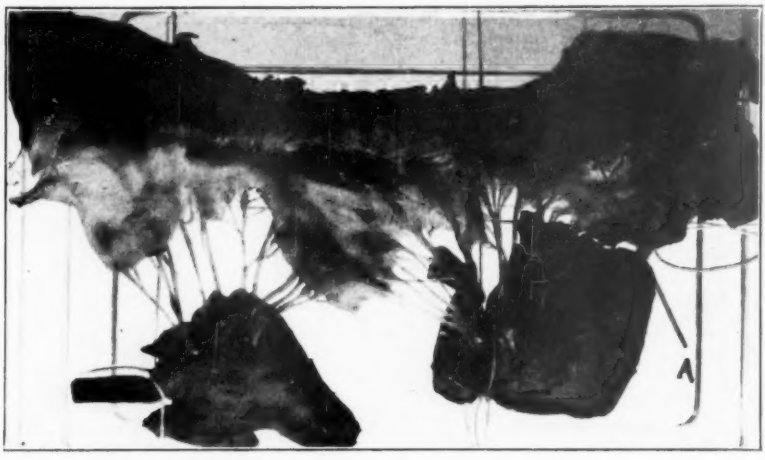

Fig. 4.—Normal tricuspid valve of the pig injected with India ink. With this magnification only the larger vessels are shown. Fig. 5 shows the details of area *A*.

without producing a superficial erosion of the endocardium. Subsequently the nodules enlarge and give rise to verrucous or villous masses, cone-shaped or pyriform, sessile or pedunculated, which are more opaque and of firmer consistence.

"In their early stage, the vegetations consist of an accumulation of lymphoid cells covered with fibrin. In this stage, the lesion can still recover by restitution ad integrum; the newly-formed masses undergo fatty-granular degeneration and are absorbed into the circulation. If this resolution does not take place, the endocardial nodules are invaded little by little by embryonic tissue springing from the squamous cells of the endocardium and from the leucocytes that have escaped from the capillaries by diapedesis. The zone of cellular proliferation is ill-defined and diminishes gradually toward the healthy tissue. On section, the vegetations exhibit at their periphery a layer of fibrin of variable thickness and in the center organized tissue composed of fusiform cells, connective tissue fibers *and embryonic vessels continuous with those of the valve.* The pathogenic bacteria are found in the meshes of the fibrinous reticulum or at the base of the granulations or in the thrombosed vessels and in the lymph-space of the connective tissue of the endocardium."

Grant[12] suggests the probability of the spread of subacute endocardial lesions by surface contact from valves to intimal lining of the aorta. Such conditions are encountered also on the endocardial surface of the auricle or ventricle where the spread may be by continuity or through anastomosis of near-by vessels.

The work of Coombs,[13] Libman,[13] Poynton,[13] Swift[15] and Clawson[14] suggest that in rheumatic fever the lesions on the valves are primarily beneath the endocardium. The process goes through the stages of active inflammation, with edema of the valve leaflet, followed by proliferation and hyalinization. The lesions occur usually at the line of

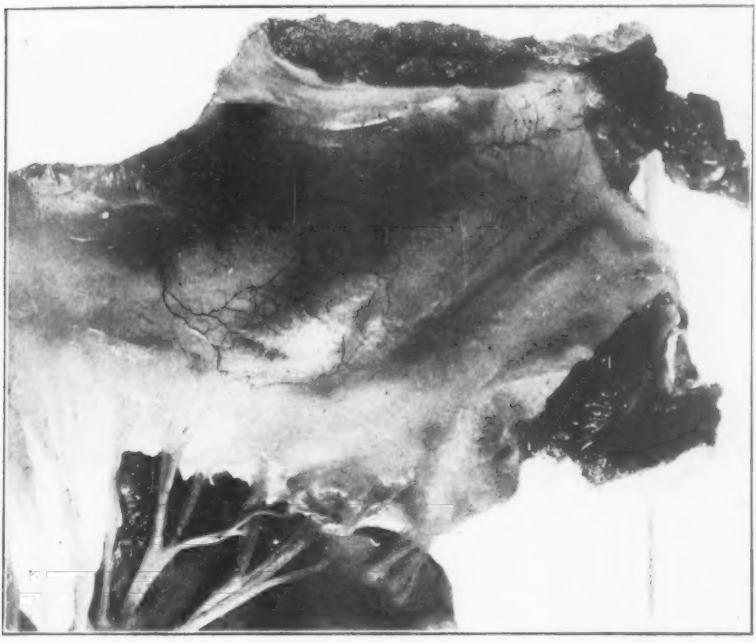

Fig. 5.—Detail of *A*, Fig. 4, tricuspid valve, showing rich vascular network at line of closure. (Free margin of valve not in focus). The chordae tendineae show some of the subendocardial vessels.

closure of the valve leaflets. The excellent work of Swift[15] on rheumatic fever shows the development of the lesions in the valve and describes them as a valvulitis.

The exact nature of the infective agent in rheumatic fever has long been in doubt. Coombs,[13] Poynton[13] and Clawson[16] state that the streptococcus is the organism responsible for rheumatic endocarditis, and suggest that rheumatic endocarditis and subacute bacterial endocarditis have a common etiology. Clawson[16] finds a positive blood culture of Streptococcus viridans in 50 per cent of acute cases of rheumatic fever, by the use of special cultural methods. Swift, however, finds

only about 8 per cent of positive cultures. If the work of Clawson can be confirmed, the suggestions made will find substantial support.

METHODS OF INJECTION

The present study of the circulation of the heart valves was begun to clear up some of the gaps in the anatomical conception of endocarditis. Previous injection studies left some doubt as to the vascularity of the chordae tendineae and the semilunar valves in the human heart.

Attempts to inject the human heart with bismuth-gelatin prepara-

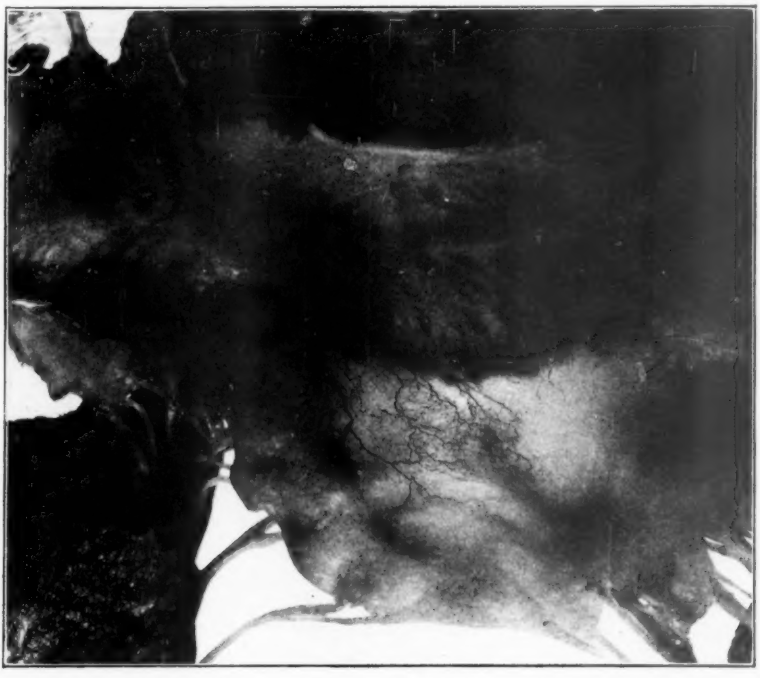

Fig. 6.—Detail of mitral valve, showing rich vascular network beyond the line of closure of the valve. The vessels on some of the chordae tendineae are also shown.

tions were unsuccessful because gelatin preparations do not penetrate the finer capillaries (Fig. 1). Celloidin injection masses likewise show only the larger vessels (Figs. 2 and 3). The valves in such instances show only the larger vessel trunks at the attachments of valve leaflets and the papillary muscles show a few small vessels.

In our studies on the pig's heart India ink, mixed with an equal amount of distilled water, has given the most satisfactory results. The injection is made through the coronary arteries at the sinuses of Valsalva under a pressure of 150-200 mm. Hg. The specimens are not washed out before beginning the injection. Care is taken to prevent the entrance of air bubbles. After the pressure has been maintained for

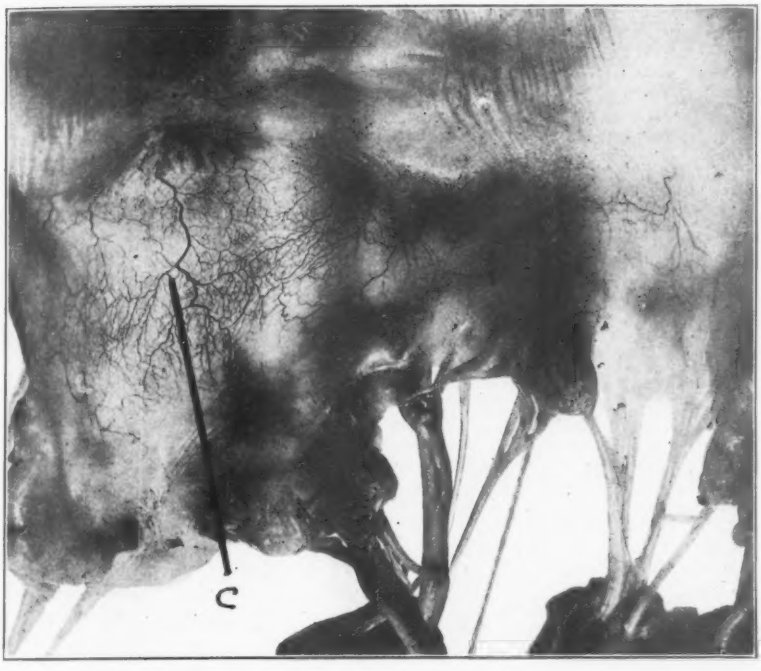

Fig. 7.—High magnification of section of mitral valve in the pig showing rich, vascular network of leaflets. Some of the vessels reach the free margin, but a few pass through the leaflets to join the branches of the chordae tendineae which are continuous with the plexus of the papillary muscles. Section removed at "C," for microscopic study, shown in Fig. 9.

Fig. 8.—Drawing of mitral valve, shown in Figs. 6 and 7. Only a few fine vascular twigs can be seen passing to the free margins of the leaflets. Deeper branches connect by way of the chordae tendineae to the plexus of the papillary muscles. (Drawing by Ralph Sweet.)

about a minute the heart is placed in formalin for fixation. Figs. 4, 5, 6, 7 and 8 show the atrioventricular valves which have been removed from such a specimen. The vessels are shown in the valve leaflet extending beyond the line of closure and continuous with the vessels along

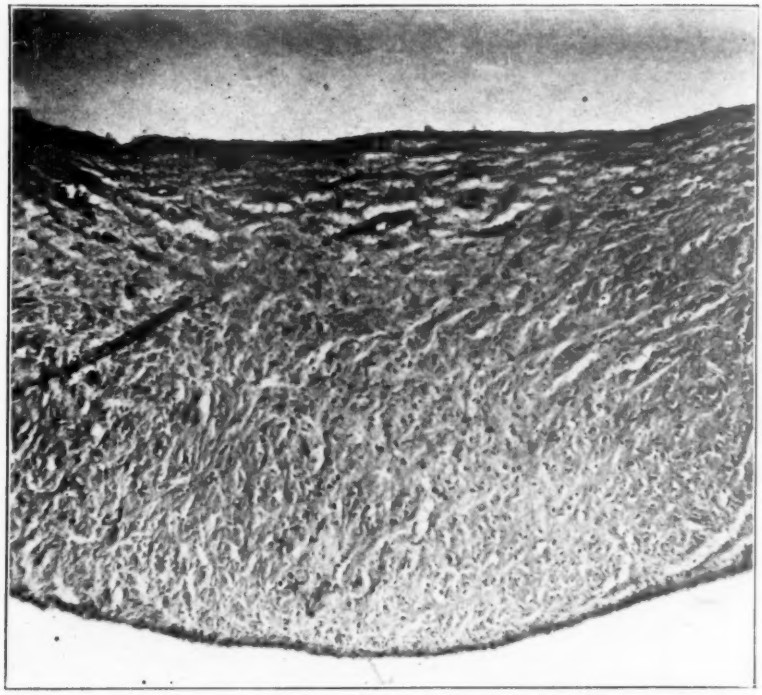

Fig. 9.—Photomicrograph of section "C," mitral valve, Fig. 7, showing India ink injection of vessels of valve leaflet. The vessels lie beneath the upper endocardial surface. The region of the line of closure is shown. (Photomicrograph by A. E. Steele, M.D.)

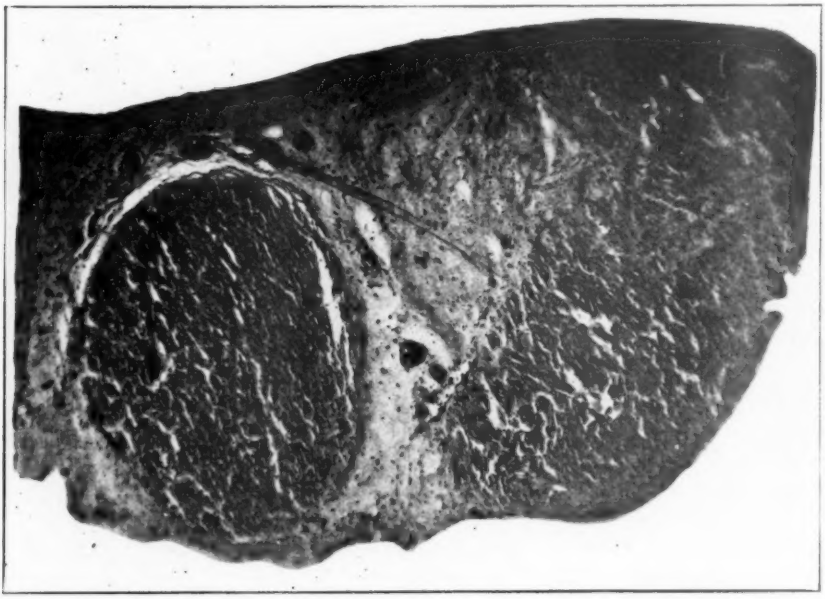

Fig. 10.—Photomicrograph of cross section of chordae tendineae of mitral valve shown in Fig. 7. Injected blood vessels are shown beneath the endocardium and between muscle bundles. (Photomicrograph by A. E. Steele, M.D.)

the chordae tendineae to the papillary muscles. Cross sections of the valve leaflet and chordae tendineae are shown in Figs. 9 and 10.

The semilunar valves are more difficult to inject, but by a modification of the technic we hope to show that the capillaries extend to the free margin of the leaflets. The injections of Bayne-Jones suggests that, with a better injection material, the complete injection is possible.

DISCUSSION

Our injection specimens of atrioventricular valves of the pig show the rich anastomosis of vessels at the line of closure of the leaflets. Smaller vessels pass to the free margin of the leaflets. The chordae tendineae are vascularized and connect the plexus of the leaflets with the plexus of the papillary muscles. The vascularity of the tricuspid valve is as great as that of the mitral valve, suggesting that either the difference in oxygen content of the blood, or the elements of pressure and trauma are also factors in the production of endocarditis.

The suggestions of Coombs and Poynton that rheumatic endocarditis is due to a streptococcus finds confirmatory proof in Clawson's excellent cultural and pathological studies. The tendency of the Streptococcus viridans to form clumps because of the cohesive nature of its capsule, as shown by Wm. H. Smith,[17] has a direct bearing on localization in the valve leaflets at the line of closure. The development of the lesion in the leaflets, as a valvulitis, as described by Swift fits in with this conception. The frequency with which subacute bacterial endocarditis "attacks" a valve previously damaged by rheumatic endocarditis would be in favor of a common etiology. The relative absence, in subacute bacterial endocarditis, of the symptoms, signs and pathological lesions in joints, meninges, pericardium, valves and heart muscle could very well be due to the reactions of tissues to the invading organism and the differences in the stages of the process. The usual manifestations of subacute bacterial endocarditis are related to the thrombotic process on the heart valves and endocardium and the systemic embolic phenomena.

The experimental production of endocarditis by Rosenow and others is significant. The increasing number of recoveries of subacute bacterial endocarditis suggest that better cultural methods are uncovering the milder types of cases.

CONCLUSIONS

1. India ink injection of the atrioventricular valves and chordae tendineae of the pig shows the relatively rich vascularity of these structures.

2. Further confirmation of the embolic conception of endocarditis is presented. Further evidence is needed to prove the identity of rheumatic and subacute bacterial endocarditis, but recent investigations are more than suggestive.

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(*For discussion see page* 123.)

AN OFFICIAL METHOD FOR LESSENING HEART DISEASE*

JOHN D. MCLEAN, M.D., PHILADELPHIA, PA.

PREVENTIVE medicine has been one of the principal functions of the medical profession, in the sick room, in the laboratory, in the medical schools and in all health agencies. This is very clearly and forcefully demonstrated by the efforts to control communicable diseases. We have so impressed the law-making bodies as to the wisdom of preventive medicine that laws have been passed giving physicians great powers over those ill and those who have been in contact with these diseases.

Health departments—international, national, state, county, and those of districts, cities, boroughs and organized communities—have been created by law giving to those departments powers which are far reaching. "Protect the masses" might well have been the slogan of the profession when these laws were urged. How great are these powers might well be illustrated by a procedure in my own state. The legislature of 1919, at the request of the Department of Health passed the following amendment: "The Department of Health may, when it deems it necessary to safeguard human life and health, declare as communicable, diseases additional to those herein specifically so declared." Immediately syphilis and tuberculosis were declared communicable diseases. In a central city of the State, in a genitourinary clinic a number of men reported suffering from syphilis; from information gained from each the source of infection was determined as coming from a certain house; this house was raided, the inmates arrested and placed in prison, only to be released within less than one hour by a court order. The inmates returned to the house, which was then placarded "syphilis"; they immediately fled the house, only to be arrested and put in prison. Much to the surprise of the lawyer interested, a court order, which called for their release, could not be obtained as the inmates now were in jail not because of being taken out of a raided house, but because they had broken quarantine.

Under these laws and regulations communicable diseases are subject to quarantine, which has been defined by the Attorney-General as meaning confinement in a room in a house, confinement in a house, or removal to an institution provided for the care and treatment of those suffering from the disease in question. This law can be enforced as it has been tested in court.

We have succeeded in decreasing the number of those suffering with

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typhoid fever and tuberculosis; typhoid, because the source of infection has been controlled; tuberculosis, because of education of the public on prevention. Part of our efforts in the past have been to educate, urge and force the adults, parents and guardians, to protect and guard the children; in this we have failed to consider those whom we wish to protect. We seem to forget that in a very few years they, the children, will be the ones who will have the power to do this; that they will be fathers and mothers and should be trained to protect their own, as we are now training *their* fathers and mothers. The communicable diseases that have not been materially lessened are diphtheria, scarlet fever, measles, mumps and whooping cough.

We have accomplished little, as we have already shown by our morbidity reports. This plan has been far from a success. If we have, therefore, failed in reducing the number of those suffering with these diseases, would it not be well to change our method and build up such a resistance within the body of each child as will lessen the number of fertile fields for their development?

This Association has two objects: (1) the prevention of heart disease, and (2) the care of those now suffering from heart disease.

There are one hundred and six million people in the United States, with about fifty-eight million over twenty-one and forty-eight million under twenty-one; of this number about four million are school children, with three million under twelve years of age. Again using my own state as an illustration, the law provides: "The medical inspectors shall, at least once each year, inspect and carefully test and examine all pupils in the public schools of their districts, giving special attention to defective sight, hearing, teeth or *other disabilities and defects* specified by the Commissioner of Health in his directions and requirements for medical inspection of schools, and shall make such additional inspections and examinations as shall be provided for in said directions or required by the Commissioner of Health, the principal, or the district superintendent of schools. Each medical inspector shall give careful directions concerning the care of each pupil who needs special care while in school. The teacher, principal or district superintendent shall carry out as carefully as possible the medical inspector's directions concerning the special care of pupils while in school."

A method for increasing resistance to these communicable diseases, which are responsible in many instances for heart disease, is as follows: First, a thorough medical examination yearly of all children between the ages of six and twelve. Under the law just quoted it is demanded; and it can, therefore, be done. Second, pay special attention to those of six years just entering school, noting carefully and fully all abnormalities and nonimmunities. Third, follow each child yearly, carefully noting conditions found and corrections made as the result

of previous years' findings and recommendations. Fourth, report yearly until age of twelve is reached. I have especially mentioned the age of twelve, as that is, as you can well realize, the age of puberty. Fifth, if done by properly trained physicians, its great value will be so appreciated by parents and educational authorities that the continuous yearly examination will be requested and demanded. The finding and remedying of defects will so increase health and resistance that germs responsible for inflammatory diseases such as heart disease will not so often find a fertile lodging place in the body. Instead of finding the disease-producing bacteria, let us so increase resistance that they will die from lack of nourishment. Let us learn the lesson taught by the tuberculosis campaign, that we have not materially lessened the number of tubercle bacilli, but have lessened the fields on which they could grow.

It is a long road, but a sure one; educate the children as to the value of medical examination and correction of defects, and all disease, including the one in which we are most interested, will be lessened.

The tuberculosis campaign took twenty years; the heart disease campaign will probably not take quite so long.

For the relief of those now suffering with heart disease a different plan must be adopted; under the law already quoted school children should be carefully examined, and if heart disease is found the medical director shall "give careful directions concerning the care of each pupil who needs special care while in school. The teacher, principal or district superintendent shall carry out as carefully as possible the medical inspector's directions concerning the special care of pupils while in school." If in the judgment of the medical inspector this care cannot be given and proper home care is not available, *hospital* care should be.

To make a plan for hospital care effective the following suggestions will help. They are applicable to any organized community.

Suggestions for State Service

I. A list of all State Institutions, in which there are patients *now*.
   (a) Location and bed capacity.
   (b) Type of patient for which it was provided.
   (c) Would the law under which the Institution is operating allow the admission of acute or chronic heart patients or both.
   (d) How is each Institution financed.
   (e) What is the procedure for admission to each.
   (f) Name of Executive Officer of each.
   (g) List of Board of Directors, or of Commission in charge.

II. A list of all State properties on which there has been no construction started.
   (a) Reason for its purchase.
   (b) List of Commissioners in charge.
   (c) Amount of money appropriated.

III. A list of all State properties on which construction has been started but not completed.

(a) To what use is each to be put.
(b) List of Commissioners in charge.
(c) Amount of money appropriated.
(d) Bed capacity.

IV. Influence legislation on a selected list of properties and institutions, so as to make them available for heart patients.

V. New legislation directing that the State purchase a site and construct buildings for the care of heart patients.

Information Valuable for Local Community Service

I. Name, and number of membership, of each Health or Welfare organization including Commissioners of the Poor.

(a) Name and address of the person most active in each organization.
(b) Name and address of the Executive Officer.
(c) Amount of present finances.
(d) What if any *active function now.*
(e) What organizations are anxious to do SOMETHING if properly advised.
(f) Find in each district one person financially able and charitably inclined toward a health improvement program.

II. Name and location of each hospital and institution which might care for acute or chronic heart disease patients, with number of beds that could be made available.

(*For discussion see page* 117.)

A NEW ELECTRODE FOR CLINICAL AND EXPERIMENTAL ELECTROCARDIOGRAPHY*

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AND
FRANK N. WILSON, M.D., ANN ARBOR, MICH.

OVERSHOOTING or fling, due to high skin resistance or a condenser effect between the skin and the german silver electrode,[1] is still a source of annoyance to many electrocardiographers. Pardee's[1] study of the causes of this source of error and of the methods for avoiding this effect have been of great value. It is, however, not always possible to reduce the high skin resistance by following Pardee's directions of thoroughly wetting and rubbing the skin of the extremity with hot (40° C. or 105° F.) saturated salt solution. In some cases, even after the removal of the skin grease with alcohol and rubbing with salt solution to the point of producing a stinging salt glow, we have encountered difficulty. The german silver plate can never be molded to fit snugly any extremity and thus produce good contact surface. Cohn's[2] lead foil electrode is a distinct improvement over the german silver electrode. Low skin resistance can almost always be attained with this small, simply constructed, easily applied and comfortable lead foil electrode. We have had fair success with this electrode modified by making it broader so that it might be molded to the extremity. The reasons for the failure of this electrode to be more generally adopted are not evident. We have had some slight difficulty with it in the working loose of the binding post and the cracking and corrosion of the lead foil.

In the planning of some experimental work in which electrocardiograms had to be taken at intervals of weeks on living dogs, it was found necessary to devise an efficient, low resistance, easily applied and comfortable, simple and sturdy electrode. It had to be one which could be applied without making an incision in the skin and without even shaving or cutting the hair from the dog's leg. Immersion electrodes such as the nonpolarizable zinc sulphate ones or the standard salt solution ones which we have used for our ambulatory cases are quite impractical for taking electrocardiograms on dogs. Likewise, german silver band electrodes or copper plate cuff electrodes[3] were found unsatisfactory chiefly because of the difficulty of fitting them to the form of the dog's leg. It was also hard to keep the electrode in place when the animal struggled a bit. High skin resistance was

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so frequently encountered that this type of electrode was considered useless.

At this juncture we decided to try Einthoven's galvanized iron wire electrode but were unable to get annealed soft iron wire that was gal-

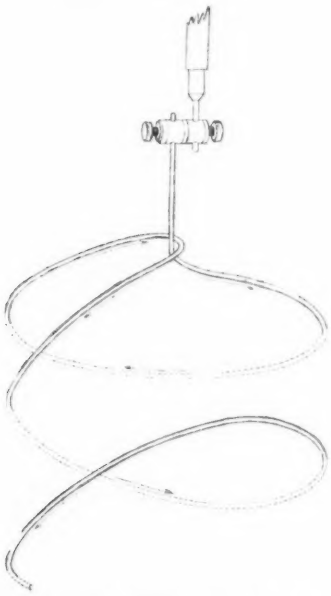

Fig. 1.—The electrode wire double binding post and end of the lead wire, illustrating the simple turns used in applying the electrode and the method of connecting the electrode to the lead wire of the electrocardiograph.

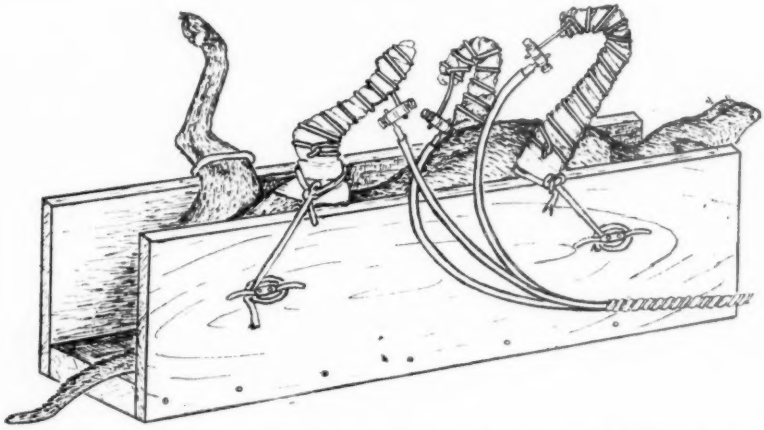

Fig. 2.—The electrodes in place on an experimental animal. The wires are wound over the wet Canton flannel salt bandages and connected with the lead wires to the electrocardiograph.

vanized. We consequently came upon the idea of trying soft copper wire, which proved to be most efficient. The soft copper wire electrode was promptly tried on bed patients and found to be in every way the

most satisfactory electrode in all cases where immersion electrodes are impractical.

The electrode consists of 16 to 20 gauge ordinary soft (annealed) copper wire and a double connecting binding post by which one end of the wire electrode may be attached to the respective lead wire of the electrocardiograph. The wire should be about a meter and a half long for

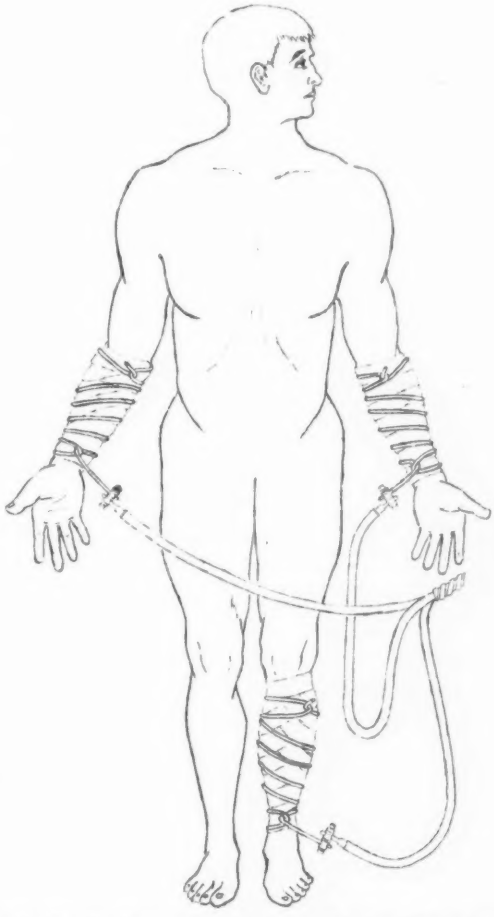

Fig. 3.—The electrodes in place on a human subject. The wires are wound over the wet Canton flannel salt bandages and connected with the lead wires to the electrocardiograph.

work on human beings and about a meter for work on animals. The extremity to which the electrode is to be applied is thoroughly soaked and rubbed with hot saturated salt solution and a strip (5 to 10 cm. wide and 75 to 100 cm. long) of Canton flannel saturated with the hot saturated salt solution is wound about the part and the soft copper wire is wound over the saline bandage and secured at either end by a loop and a bending back of a short piece of the wire. The electrocar-

diographic lead wire is attached to either end of the copper electrode wire by the double connecting binding post.

This electrode meets all the requirements for an efficient electrode. The skin resistances are uniformly low (500 ohms and less). It is, in our experience, by far the easiest to apply, the easiest to keep in place, the easiest to keep in order, the simplest and cheapest to make and consequently the electrode of choice.

The usefulness of this electrode in clinical cardiology is evident in the success of those clinicians who have adopted it and discarded the german silver plate type, which is supplied with electrocardiographic outfits as standard equipment.

In experimental work it has proved to be an even greater boon, since it makes it unnecessary to incise the skin, to shave or cleanse the skin or even to cut the hair from the dog's leg. Then, too, it is especially useful in work on unanesthetized animals, since it is comfortable and remains firmly in place in spite of struggling, some of which is often unavoidable. Furthermore, in the case of a dog, the Canton flannel saturated with strong salt solution can be wound over the foot pads of the animal and fixed in place by the copper wire electrode, thus insuring the best possible contact.

We are indebted to Dr. Morell W. Miller for the illustrations.

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The American Heart Journal

VOL. I ST. LOUIS, MO., OCTOBER, 1925 NO. 1

Official Organ of the American Heart Association

Editorials

The American Heart Journal

The past few years have witnessed so great an increase in the number of periodicals the interests of which are limited to single, special fields of medicine that the appearance of still another special journal seems to call for a word of explanation.

Many things have conspired to bring about the very widespread interest in circulatory diseases which is now so apparent; but of these, much the most important has been the truly revolutionary advances made in our knowledge of the normal and pathological physiology of the heart and its beat, along with the advance in understanding of its diseases and their management. Moreover, this newly awakened interest in disorders of the cardiovascular system has led to a realization of the problem of heart diseases as extensive and important public health relations which cannot longer be disregarded. This feeling has found expression in the establishment of a national organization dedicated to the prevention and public health aspects of such diseases.

The rapid extension of interest in the various phases of cardiovascular disease has been accompanied by a vast amount of writing upon the subject and these publications at present are scattered widely through the general medical literature and are not easily available. Some means of concentrating and focussing all this new and important information is urgently needed.

The AMERICAN HEART JOURNAL is the resultant of the action of two distinct forces; one the increasingly evident demand by physicians throughout the country for a periodical covering the field of diseases of the heart and circulation, and the other the conviction on the part of the American Heart Association that such a journal might be made a potent factor in the furtherance of its purposes; for the better education of the medical profession in matters relating to the diagnosis, treatment and prevention of heart diseases is the first essential step in the campaign against these diseases. The new journal is designed to serve not merely the limited group of heart specialists, but the very much larger class of intelligent well-trained general practitioners who aspire to keep abreast of the rapidly growing knowledge of the heart and its disorders. The AMERICAN HEART JOURNAL, although primarily clinical in character, will attempt to cover all phases of the subject of cardiovascular diseases. Its original articles, in addition to clinical studies, will include those embodying the results of special research and those dealing with the public health aspect of the subject. Through its Abstract Department it will try to provide its readers with the essential facts of all the more important articles in current literature relating to its special field. It is hoped that these abstracts, together with frequent critical reviews of the literature upon special phases of cardiac diseases, may be a useful and attractive feature.

The AMERICAN HEART JOURNAL bespeaks the support and aid of everyone interested in securing progress in our knowledge of the circulatory diseases and of their relief and prevention.

—*L. A. C.*

Society Transactions

AMERICAN HEART ASSOCIATION

MEETING OF MAY 26, 1925

DR. JOHN D. MCLEAN, of Philadelphia, read a paper entitled **An Official Method for Lessening Heart Disease.** (For original article, see page 107.)

DR. JOSEPH SAILER, of Philadelphia, read a paper entitled **The Care of Adults with Moderate Heart Disorders.** (To be published later.)

DR. JAMES G. CARR, of Chicago, read a paper entitled **The Economic Phases of Cardiac Disease.** (For original article, see page 62.)

DISCUSSION OF PAPERS BY DRS. MCLEAN, SAILER AND CARR

DR. W. S. THAYER, BALTIMORE.—One word with regard to the observations of Dr. Sailer on the importance of a thorough and careful examination. A recent experience emphasizes this. A college student who regarded himself as perfectly well came up for a routine physical examination. He had been examined every year for six or seven years in school or college and the heart had been regarded as normal. He had had no suggestive symptoms. He had a complicated, remarkable congenital heart disease with a very large heart, the apex away around in his axilla and a loud murmur, most intense in his tricuspid area. His enlarged heart however had never been noticed and his murmur had never been heard. Why? Simply because the murmur entirely disappeared in the erect posture but was intense when he lay down.

Then as to the importance of making a really thorough examination when one desires to employ more elaborate methods. Polygraphic tracing was taken which showed an A-C time of .3 of a second, but the electrocardiogram showed that his P-R time was .11 of a second. The picture was most complicated and paradoxical, and difficult of interpretation, but it emphasizes so well the way in which important data may be missed in the simple example of the patient if one does not take the pains to examine as a routine, size and position of the heart and always to examine the patient in the erect and the recumbent posture and secondly it emphasizes how easy it is to be misled in a more careful study if we do not employ all the means at our disposal.

DR. THOMPSON FRAZER, ASHEVILLE, NORTH CAROLINA.—The program as just outlined is very much like that which has been carried out in the management of cases of tuberculosis. In both conditions we are dealing with a chronic affection; in both there is the tendency to relapse if the patient is not under supervision for a sufficient length of time, and in both there is the economic situation which goes with a chronic disease and the attendant loss of earning power. The progress which has been made in the treatment of tuberculosis has

been possible only through the organized efforts of the National Tuberculosis Association; heart disease, which presents similar problems, must also be combated by organized effort.

DR. HAVEN EMERSON, NEW YORK CITY.—It is quite inconceivable that cardiac disease as we believe it should be diagnosed, can be detected in the course of routine medical inspection of school children. Parents will have to take on themselves responsibility for thorough health examinations of their children in the pre-school years, without waiting for the usually hurried inspection of the school doctor who may have as many as 13,000 children to supervise.

DR. JAMES HEARD, PITTSBURG.—In Pennsylvania, examinations of school children is hampered by a law which forbids school inspectors from having the chests of school children bared for purposes of examination unless written consent of parents is obtained. The application of this law practically prohibits the making of a satisfactory examination. Under these circumstances, the title "school inspector" is an accurate one. Before changing the title of school inspector to that of school examiner, this pernicious law should be repealed.

DR. NEUTON S. STERN, of Memphis, read a paper entitled **Hypertension in the South,** of which the following is an abstract.

A comparison of statistics gathered from a number of hospitals in different parts of the country with reference to the incidence of cases of arterial hypertension gave conflicting results and furnished little information of value. Among a series of 200 personally studied heart cases in Memphis, the incidence of hypertension was nearly 50 per cent. The greatest number of such hypertension cases were seen in the sixth decade of life and the ratio of women to men was as three to two.

DRS. S. A. LEVINE AND F. C. NEWTON, of Boston, presented a paper entitled **The Selection of Patients with Angina Pectoris for Sympathectomy, with a Report of Additional Cases.** (For original article, see page 41.)

DR. PAUL D. WHITE, of Boston, and DR. MERRILL M. MYERS, of Des Moines, read a paper entitled **The Classification of Cardiac Diagnosis, with Especial Reference to Etiology.** (For original article, see page 87.)

DSCUSSION OF PAPERS BY DRS. STERN, LEVINE AND MYERS

DR. W. S. THAYER, BALTIMORE.—As Dr. Levine has said the diagnosis "angina pectoris" is only the expression of a clinical syndrome. The duty of the physician is to seek out the cause of this syndrome in the given case. My own experience with the operation is slight. But one of my patients has been operated on. This was a man who had angina for a year or two, at the outset. typical angina of effort, gradually increasing, until at length he was bedridden—the slightest movements associated with pain. The heart was of normal size; there was no modification of the blood pressure; the electrocardiograms showed no abnormalities. Having reached the stage where his life was a burden, where even the simplest efforts brought on his symptoms, the three ganglia on the left were removed by Dr. Finney under general anesthesia. The operation was well

borne, but in a few hours the pulse became exceedingly rapid and the patient died. The necropsy showed a coronary sclerosis with extensive fibrosis of the heart muscle, the affected areas lying deep in the ventricular muscle, not involving the conducting tract.

DR. B. S. OPPENHEIMER, NEW YORK.—In the present state of our knowledge of the surgical treatment of angina pectoris, it is most important to accumulate the records of as many cases as possible. It is necessary to know not only the ultimate results following the operative procedure, but also the details of the medical treatment employed *before* radical measures were attempted. Dr. Levine has collected some ninety recorded cases. I have had the opportunity of seeing from the medical standpoint some of the cases operated by Dr. Howard Lilienthal in the course of the past eighteen months. Briefly, the results of five cases so far have been as follows: In two cases, very satisfactory; in two, recurrence of the anginal attacks; the remaining case was atypical, and the effect of the operation is doubtful owing to psychic factors. In all but one, the patients had not responded to medical treatment, including very considerable limitation of their field of activity. General anesthesia was usually, but not invariably, employed. The operation in general was cervical sympathectomy; the exact portions of the nervous system resected varied from case to case. In the majority of cases unilateral cervical sympathectomy was not sufficient, and the opposite side had to be operated at a subsequent session. No attempt was made to find the so-called depressor nerve; in fact the sheath of the neurovascular bundle was not even opened. Connections of this nerve may, however, have been damaged in the course of sympathectomy; but if so, this was accidental. (Even in the hands of Dr. Hofer of Vienna the so-called depressor nerve has not been found at operation in every case.) There was no mortality, but Dr. Lilienthal has refused to operate upon any case which showed evidence of myocardial involvement.

In very carefully selected obstinate cases,—especially avoiding if possible all such in which *any* operative procedure would be precarious,—I think it is worth while tentatively to pursue the surgical treatment of angina pectoris. Whether this should be along the lines of cervical sympathectomy introduced by Jonnesco, Coffey and Brown, or of section of the depressor or vagus nerve as suggested by the Viennese School (Wenckebach, Eppinger and Hofer) is a very open question.

DR. HAROLD FEIL, CLEVELAND.—I wish to report one case of angina operated with relief of symptoms. The patient, a man of seventy-four years, with moderate arteriosclerosis, had substernal pain of such severity that he craved any procedure that promised some amelioration of pain. The left superior and middle cervical sympathetic ganglia were removed by Dr. A. Strauss. Since the operation, he has been almost completely free from pain, walking two or three miles without symptoms. While he still has occasional pain, he lives a life of comparative comfort.

DR. EMANUEL LIBMAN, NEW YORK.—Dr. Levine has properly stressed the importance, particularly at the present time, of selecting the cases for operative treatment with great care. Patients who have survived an attack of coronary thrombosis, whether they present clinical symptoms or not, are poor operative risks. It must be remembered, however, that even in the absence of thrombosis, obstructions and stenoses of the coronary arteries may result in severe cardiac accidents which may be suddenly fatal. It is not infrequently difficult, even when electrocardiographic aid is available, to differentiate such cases from those in

which a thrombosis has caused occlusion. Moreover, this may take place insidiously, as it so often does in arteries in the lower extremities. The necessity for care in the choice of cases for operative therapy is made still more clear by the fact that it may happen that in a case which is subjected to operation, death may occur upon the table, and no lesions of any significance be discovered in the aorta, the coronary arteries or the heart.

It is because of the difficulties which are at times encountered, in the attempt to distinguish coronary artery thrombosis from other conditions giving a more or less similar clinical picture, that I will today present a paper dealing with the diagnostic value of blood examinations. It does not appear to me that one can make a division of coronary thrombosis and one of angina pectoris. If the latter term is used at all, one should add to it the cause, if that be discoverable. If the term is to be used in the sense in which Dr. Levine has suggested, it should in my opinion be restricted to those cases in which the clinical picture is not accompanied by evidences of a lesion in the heart or arteries and in which the clinical inference is that the symptomatology is due entirely or in much the larger part to a disturbance, organic or functional, in the cardiac nerves. In such cases, even though the attacks of pain are often very severe, increased discomfort on exercise is inconspicuous. At the postmortem examination of some of the cases of this type, however, one may be surprised by finding lesions which can be held more or less accountable for the sufferings of the patient. This subject cannot be much clarified until we know more of sensitization of the cardiac nerves with or without evident lesions in them. It appears to me that the cases which are at the present time best adapted for trials of operative therapy are those in which the nerve element is the outstanding factor, and cases of hypertension accompanied by insufferable pain not relieved by other methods.

DR. LEWIS A. CONNER, NEW YORK.—I think we will all agree with Dr. Levine as to the urgent need for a careful and discriminating selection of patients if this operation is to be considered. I am quite in accord with Dr. Libman, however, in feeling that it is difficult, or often impossible, to distinguish between the cases which Dr. Levine classes as those of true angina pectoris (accepting, I presume, the views of Allbutt) and cases in which the pain is due to impairment of the coronary circulation. I find myself often quite unable to make the distinction; but certainly in most of the patients that I see, the course of the disease indicates that the pain has been the result of coronary disease rather than of occult changes in the aorta. Because of this inability to distinguish between these two classes of cases, I have been loath to recommend operation and have had no personal experience with it. In instances in which the pain is so intolerable that life is not worth living, I think the operation is quite justifiable, but in the common type of patient in whom the pain is always, or usually, the direct result of physical exertion, I have looked upon the pain as an indication of inadequate coronary circulation and as, therefore, a warning signal of some importance. The removal of that signal would be very unlikely to benefit the underlying condition, but rather would tend to make a bad matter worse. It might be compared to the cutting of the sensory nerves of the breast to cure carcinoma.

DR. S. A. LEVINE (closing).—It is well to bear in mind that these patients are all alive and not dead. The point I mean to bring out is although we may not be able to predict in all instances, I think we are able to tell, generally, who is having cardiac infarction and who is having angina pectoris; and in the former cases, the operation should be done. It affords great comfort to some patients and I am not at all concerned that removing the signal of pain that the patient uses, is doing him any harm. He may even have a greater longevity.

Dr. F. A. Willius and S. F. Haines, of Rochester, Minnesota, presented a paper entitled **The Status of the Heart in Myxedema.** For original article, see page 67.)

Drs. W. J. Kerr and S. R. Mettier, of San Francisco, presented a paper entitled **The Circulation of the Heart Valves. Notes on the Embolic Basis for Endocarditis.** (For original article, see page 96.)

Dr. E. Libman, of New York, read a paper entitled **The Importance of Blood Examinations in the Recognition of Thrombosis of the Coronary Arteries and Its Sequelae,** of which the following is an abstract.

The most common causes of pain in the cardiac area, of the type of so-called angina pectoris, are hypertension, dilatation of the ascending arch of the aorta, with or without atherosclerosis, and disease of the coronary arteries. In a given patient, one or more of these conditions may be present. Cases in which the characteristic pains occur, and in which the pathological investigation reveals no lesions to which they can be ascribed, are, to say the least, uncommon. In such cases pain on exertion may be slight or absent.

The diseases of the coronary arteries that are most significant are narrowing or stenosis of one or both coronary arteries, especially at the ostia, and thrombosis. The latter may occur in association with marked atherosclerosis or calcification, or both, or in vessels that show little change. Thrombosis is, on the whole, the most serious of the conditions named, although patients suffering from narrowing or stenosis, especially at the ostia, in the absence of thrombotic processes, may die more or less suddenly. The nausea and vomiting so characteristic of attacks of thrombosis may be present.

The recognition of coronary thrombosis is often clear enough in those cases in which the characteristic symptoms are present, and especially if electrocardiographic evidence of a recent occlusion is found. But when the picture is incomplete there may be great difficulty in determining whether a thrombotic condition is present or not. The difficulty is particularly marked in those cases in which there is little or no pain. Such a picture occurs usually in patients who are naturally hyposensitive to pain. The clinical phenomena of coronary thrombosis in such hyposensitive persons are atypical and very varied.

Many years ago it occurred to me that when a necrosis of the myocardium took place it should be accompanied by a polynuclear leucocytosis, and that such a change in the blood would be of diagnostic value. In other words, if after an attack of severe and radiating pain in the cardiac area, a leucocytosis ensued, that would indicate necrosis of the myocardium, and by inference coronary thrombosis, because such necrosis is nearly always the result of infarction due to closure of a coronary artery. On making studies with this idea in mind, I learned that the appearance of a leucocytosis was of the greatest value, far more so than pericarditis, (so-called pericarditis epistenocardica), which is much less often clinically apparent.* I also found that while the leucocytosis may go hand in hand with elevation of temperature, it was often discoverable before the temperature rose, or when fever did not develop.

*Observations relative to this subject have been made by Levine and Trattner, Wearn, Loewenberg, and others.

The leucocyte counts which make the basis of my report were performed at varying times after the onset of the attack of thrombosis. It is important not to wait too long before making the blood examination because a pulmonary inflammation or infarction may set in, which of itself causes a leucocytosis. Massive collapse, which occasionally occurs at the onset of a coronary thrombosis, is not accompanied by leucocytosis unless it becomes the seat of an inflammatory condition.

The counts of which I have kept records vary between 9,200 with 81 per cent, and 25,500 with 83 per cent, polymorphonuclear leucocytes. In somewhat over one-half of the cases the leucocyte count is between 15,000 and 20,000. The lowest percentage of polynuclears was 78, and the highest 91.

It is of course possible that thrombosis with infarction may occur in the absence of leucocytosis. I have no record of such a case. According to my experience the leucocytosis when present is due to infarction. I have no proof that thrombosis alone can produce this change in the blood, but there is valuable evidence which proves that infarction alone can be responsible. This evidence is in the nature of observations on two cases of recent necrosis of the heart muscle, accompanied by leucocytosis, and associated with only old occlusion in the coronary arteries. The pericarditis (which is rarely extensive) seems to play little or no rôle in the development of leucocytosis.

A leucocytosis may be found as early as one hour and forty-five minutes after the onset of the symptoms in a case of thrombosis, and may then already be as high as 20,000 or more. As the elevation in the number of leucocytes is so early evident, it has no value in the differentiation of coronary thrombosis from such abdominal conditions as acute hemorrhagic pancreatitis and cholecystitis, in which marked leucocytosis is often found very early. It has, however, a significance in the differential diagnosis of coronary thrombosis and such confusing abdominal conditions as are not accompanied by leucocytosis. Apparently the most favorable time at which to examine the blood is between six and twelve hours after the beginning of the attack.

If the leucocytosis does not markedly recede within a few days, or if it increases with or without a preliminary decrease, and there is no complication which explains its persistence, we must suspect that a progressive necrosis or an intraventricular thrombus, or both, are present. Intraventricular thrombosis is much less common than myocardial infarction. It may accompany the latter, but is much more apt to occur much later, especially when there results a chronic aneurysm of the heart. Such intracardiac thrombosis may, by itself, bring on a leucocytosis as high as at least 24,200. Progressive necrosis is accompanied by the possibility of the development of an acute aneurysm of the heart, and of rupture of the heart.

It is necessary to note that when hemorrhagic infarction of the lungs develops, a leucocytosis occurs which may be very marked. In one of my cases the count was 34,000, with 97 per cent polymorphonuclear leucocytes. We need observations of blood counts in pulmonary edema, especially as it may be practically the only definite clinical manifestation in a case of coronary thrombosis. In cases that have recovered from an attack of thrombosis and consequent infarction, there may be present a lymphocytosis and also a leucopenia.

The examination of the blood for leucocytosis is valuable to the practitioner in the recognition of the usual types of coronary thrombosis, and as an aid in prognosis and management. The patient who has suffered an infarction, other things being equal, needs much longer rest in bed than patients whose symptoms are due to other causes, unaccompanied by myocardial necrosis. The presence of a leucocytosis is also valuable when a sharp attack occurs in a case in which

there is known to be present an old occlusion, and in which it is essential to determine whether the attack is the sequel of the old closure, or whether it is due to a recent thrombosis. The same holds true for cases in which a chronic aneurysm of the heart, due to a former thrombosis, is present.

DISCUSSION OF PAPERS BY DRS. WILLIUS, KERR, AND LIBMAN

DR. W. S. THAYER, BALTIMORE.—Let me congratulate Dr. Kerr on this beautiful piece of work. The demonstration of so extensive a circulation in the cardiac valves together with Swift's observations showing that the early stages of the so-called rheumatic endocarditis lie in perivascular inflammatory processes, in the substance of the valves themselves and associated with considerable edema, raise the question as to whether some of the systolic murmurs heard early in an attack of rheumatic fever may not after all depend upon the valvular affection rather than on myocardial dilatation.

DR. EMANUEL LIBMAN, NEW YORK.—It seems to me that it would not be proper to let Dr. Kerr's clear presentation of his valuable study pass without further comment. A discussion of the experimental results would be without point,—they speak for themselves. I do want to say something, however, in connection with what Dr. Kerr said concerning rheumatic endocarditis. Streptococci of anhemolytic character (so-called Streptococcus viridans) are being found more and more often in the blood in cases of rheumatic fever. We do not yet know what rôle these organisms play. Kinsella and Swift, who made some of the earlier studies, could not demonstrate any immunological response to their presence. If it were proved that these streptococci were really important from the etiological standpoint, it would be difficult to explain why they are not demonstrable in the Aschoff lesion. The latter would have to be considered to be only toxic in origin. From certain observations it appears to me that the nasopharyngeal mucous membrane is an important, perhaps the original, seat of the virus of rheumatic fever, and that the intestinal tract (colon) is at least occasionally another localization.

DR. W. S. THAYER.—Dr. Libman has mentioned casually the instances of massive collapse of the lung. I have seen but one such case. There is one thing however, which is exceedingly important from a diagnostic standpoint, namely, that the mediastinal contents, including the heart, are displaced immediately toward the affected side. This is in most instances the key to the diagnosis.

DR. LIBMAN (closing).—Dr. Thayer's point is of course correct. One is rather hesitant to subject those patients who are in the midst of a severe attack, to any method of examination that may disturb them.

Department of Reviews and Abstracts

Selected Abstracts

Henderson, Yandell and Haggard, Howard H.: The Circulation and Its Measurement. Am. Jour. Physiol., 1925, lxxiii, 193.

These authors describe in detail the importance of determinations of the total blood volume. They review the work which has been done by other workers along this line, pointing out the various advantages and disadvantages associated with each method, particularly in determining the blood volume in human beings during health and exercise. They have devised a method which consists in determining the absorption of ethyl iodide, a volatile liquid which is fixed in the body tissues, and the absorption of which can be measured. The method for determining the amount of ethyl iodide in brief, is the same as that for the estimation of ethyl ether by oxidation by iodine pentoxide. They state their belief that this method is accurate, is easily applicable to human beings and may be carried out in any ordinary clinical laboratory.

The results which they have obtained for measuring the circulation in man by means of ethyl iodide is based on the determination of four quantities: (1) volume of air inspired per minute; (2) the concentration of ethyl iodide in this air; (3) the concentration of the substance in the expired air; (4) the concentration in the alveolar air. The first factor is multiplied by the difference between the second and third and gives (*a*) the amount of ethyl iodide absorbed per minute. The fourth factor is multiplied by the coefficient of solubility and gives (*b*) the amount of arterial blood. Then *a* divided by *b* gives the volume of the blood flow through the lungs—in other words the circulation. They describe again a device for obtaining alveolar air by a method which is easy of application to clinical conditions.

The most significant findings they have reported relate to the stroke index, or volume in cubic centimeters of blood per kilo of body weight discharged by the heart at a beat, and the arterial venous oxygen difference. They find that the stroke index in normal persons during sitting rest ranges from 1.3 to 1.8. In some individuals it is much larger in the recumbent position,—up to 2.0 or more; and much smaller in the standing position,—down to 1.0 or less. During vigorous exercise the stroke index may rise to about 3.5.

The oxygen difference as shown by their results would indicate that the blood stream pumped by the heart is about twice as large as was formerly supposed. During body rest its volume in liters per minute is about equal to the volume of air breathed per minute. During exercise the respirations may increase 8 or 10 fold, and the circulation 4 or 5 fold.

If the method proves to be applicable to clinical conditions and can be made accurate, then this contribution marks a noteworthy step in our study of the circulation in man and will lead to a more satisfactory understanding of the physiological processes of the heart.

Gordon, Burgess; Matton, Mercel; and Levine, S. A.: The Mechanism of Death from Quinidine and a Method of Resuscitation: An Experimental Study. Jour. Clin. Investigation, 1925, i, 497.

As a result of experiments on cats, the M.L.D. of quinidine bisulphate was found to be dependent upon the speed of administration. There was a striking fall of blood pressure following nonlethal doses. The respirations were temporarily but briefly abolished and with increasing doses there was a slowing of the rate and a decrease in the depth of inspirations. The heart continued to beat after complete respiratory failure.

When the respirations had stopped even for a period of one or two minutes they could be revived satisfactorily by artificial respiration combined with the use of caffein sodium benzoate (5 mg. per kilo, intravenously). The caffein alone was frequently sufficient, although artificial respiration alone was much more effective.

The appearance of the animals and a study of their hearts indicate a grave intoxication of the heart muscle. Fibrillation of the ventricle was very rarely observed.

Resnik, Wm. H.: Transient Auricular Fibrillation following Digitalis Therapy, with Observations upon the Reaction to Atropine. Jour. Clin. Investigation, 1924, i, 181.

Seven colored patients in the wards of the Johns Hopkins Hospital suffering from an advanced degree of myocardial failure showed transient auricular fibrillation as a result of digitalis medication. The rhythm became normal a few days after the withdrawal of the drug, having produced no appreciably harmful influence upon the patient's course.

The response to atropine showed that the auricular fibrillation was due in some cases to strong stimulation of the vagus nerves, but that in most instances it was due to direct action upon the heart muscle. In one patient there was a reversion to normal rhythm following the use of atropine.

Myocardial failure is an important, probably necessary predisposing factor in the production of transient auricular fibrillation by direct action on the heart muscle, and possibly by the vagal action of digitalis.

Barach, Jas. H.: Arterial Hypotension. Arch. Int. Med., 1925, xxxv, 151.

The author found the incidence of arterial hypotension fairly constant, being about 3.5 per cent of persons in good health. The subjects are distinctly undersized, physically subnormal, are nonathletic and are of the hyposthenic or asthenic type. They have narrow nostrils, and frequently nasal obstruction; they have narrow chests and slender bodies. They have a smaller than normal chest capacity. They have a marked tendency to muscular relaxation, frequently have drooping shoulders and they are shallow breathers. It is his strong impression that the subject is endowed with a poor respiratory apparatus.

He states that there is a relationship between hypotension and the distribution of oxygen in the tissues. In acute infectious diseases, involving the respiratory tract, in which a respiratory deficit occurs; in chronic pulmonary diseases, and in metabolic diseases in which there is a subnormal oxidation, and in other diseases in which there is an insufficient volume of blood to carry oxygen one finds arterial hypotension. Also when newcomers first reach a high altitude there is a fall in blood pressure. This fall is quickly compensated by those individuals who have a good response to respiratory effort and oxygenation.

Dieuaide, Francis R.: The Electrocardiogram as an Aid in the Diagnosis of Adhesive Pericardial Mediastinitis. Arch. Int. Med., 1925, xxxv, 362.

It has been known that in normal persons, on changing the position of the subject there is a change in the form of the electrocardiogram as secured in the three usual leads. This is especially prominent in patients with cardiac disease and is best seen on turning the individual in the reclining position from one side to the other.

Fifteen patients have been studied in the series, eight of whom came to autopsy. The electrocardiogram showed no significant change with a shift in position. All were found to have important lesions involving both the pericardium and the mediastinum. Of a larger series of patients with clinical signs of "adherent pericardium" whose records showed a marked change, none was found to have lesions both of the pericardium and of the mediastinum.

The author suggests that fixation of the electrical axis determined by this means, may serve as objective evidence of this lesion.

Thayer, Wm. S.: Notes on Acute Rheumatic Diseases of the Heart. Bull. Johns Hopkins Hospital, 1925, xxxvi, 99.

An analysis is presented of twenty-five cases of acute or subacute endocarditis coming to necropsy within the last thirty-five years at the Johns Hopkins Hospital, which appeared to be of indisputably pure rheumatic origin without demonstrable complicating bacterial septicemia. The various points which usually are noted in connection with rheumatic disease of the heart have been observed in this series of cases. Those points which need emphasis, particularly since they confirm, again, previous ideas are: (1) the manner of onset. In a surprisingly large proportion of cases the arthritic symptoms were slight. The disease was one of the heart rather than of the joints. Especially significant was the presence of unaccountably persistent fever in association with chorea and mild atypical arthritis. (2) Petechiae were not observed in a single one of these twenty-five cases. The other common signs of subacute endocarditis were also lacking. (3) Acute myocarditis is described as a characteristic feature of acute rheumatic heart disease, occurring in 92.5 per cent of the cases. The essential myocardial lesions described are the peculiar and distinctive perivascular foci of cellular infiltration and subsequent scarring. (4) While the etiological element was not apparent, the sequence of the disease to acute tonsillitis and nasopharyngeal infections was striking. (5) Mitral insufficiency in the early stages of the disease is probably in most instances dependent on muscular relaxation due to myocardial changes. Only later with endocarditis and scarring are the endocardial changes sufficient to produce essential valvular changes.

Karsner, Howard T.; Saphir, Otto; and Todd, T. Wingate: The State of the Cardiac Muscle in Hypertrophy and Atrophy. Am. Jour. Path., 1925, i, 351.

These workers have selected hearts which showed, as far as possible, simple hypertrophy, atrophy, and normal heart muscle tissue. By standardized serial sections and microscopic examination they have measured the number of cells and nuclei and the diameter and appearance of individual heart cells. Their results present the interesting fact that the number of fibers per given area of muscle tissue is about the same in normal and atrophic hearts. In hypertrophic hearts there are many less. The breadth of the fiber is also about equal in normal and in atrophic hearts, whereas they are much larger in hypertrophic hearts. It is interesting in this connection to note that the mean number of large fibers in the hypertrophic heart is far greater than those which are normal or small in size.

Correspondingly, in the atrophic heart, the mean number of small fibers is much greater than of those which are normal or large, whereas in the normal heart there is the usual "scatter." As would be expected, the number of nuclei per field in the hypertrophic heart is less than in the normal heart. The number of nuclei in the atrophic heart is much increased.

It seems probable from their observations that the total number of fibers in the hypertrophic heart is about the same as in the normal. In the atrophic heart, however, the total number is reduced and this reduction is at the expense of the larger and smaller fibers. The changes in the atrophic heart are associated with retrogressive processes. In discussing the variability of the breadth of fibers they state that this tendency toward uniformity is an adaption to abnormal demands, and thus furnishes a new conception of the place of variability in adaption. This work confirms observations made by previous workers and should be of help in consideration of clinical hypertrophic and atrophic hearts in relation to exercise.

Gilbert, N. C.: Examination of the Heart in Industry. Jour. Industrial Hygiene, 1925, vii, 105.

The attitude of the employer towards individuals with heart disease is taken up in detail. Methods of examination and a classification of those individuals who have heart disease are given. They are grouped into three classes: (1) those who have evidence of anatomic changes in the heart, but no evidence of loss of function. Such individuals are given employment adjusted to their heart tolerance. (2) Those whose hearts have been damaged to the extent that there are some signs of cardiac insufficiency and who do not show normal response to effort, but in whom infection can be ruled out. They too may be given employment adjusted to their tolerance. (3) Those who show evident heart disease, but who in addition show evidence of a present infection. Stress is placed on this class as being unfit for any form of employment.

The author considers as well syphilitic infection of the heart and emphasizes the fact that this offers a much more difficult problem for the employer. He discusses the relation of individuals suffering with the symptom-complex termed "effort syndrome" to employment. His exact disposition of this class of people does not leave clear what should be done with them. They represent a large group who apply for work and the differentiation from structural heart disease, as is known, may be very difficult. Many of these need employment to gain livelihood. Unquestionably, further reports similar to this will be needed to bring out all the points in this connection.

Riecker, Herman H.: A Clinical Study of Quinidin Therapy. Amer. Jour. Med. Sci., 1925, clxx, 205.

The author reports the method of treatment of auricular fibrillation with quinidin in fifty-two cases and his results. The plan of treatment consists in the preliminary thorough digitalization of the patient, complete rest in bed and other measures necessary to bring the heart to the best possible degree of compensation. The pressure of fever must be avoided. The digitalis is then discontinued and the administration of quinidin begun in 0.4 gm. doses every four hours day and night.

All the cases upon which the study is based have been chronic auricular fibrillation, with the majority, definite valvular damage of rheumatic endocarditis. Forty-one of the fifty-two consecutive cases treated, or about 79 per cent resulted in restoration of normal rhythm, six cases had normal mechanism for more than a year, and twelve for more than six months.

The author divides the cases of failure to respond to treatment into two groups: (1) faulty administration of either digitalis or quinidin or both and (2) improper management of the cases with reference to exercise or mental excitement or the pressure of fever.

In thyrotoxicosis complicated by cardiac decompensation and auricular fibrillation quinidin treatment is definitely indicated. The contraindications usually to be heeded are (1) special sensitiveness to the physiologic action of the cinchona compounds; (2) a recent history of embolic phenomena; (3) marked decompensation of the heart.

The author's experience leads to an optimistic attitude toward the use of quinidin in auricular fibrillation.

Swift, Homer F.; Miller, C. Phillip, Jr.; and Roots, Ralph H.: The Leucocyte Curve as an Index of the Infection in Rheumatic Fever. Jour. Clin. Investigation, 1924, i, 197.

The leucocyte curves of twenty-eight patients with active rheumatic fever were studied for a sufficiently long period of time to be included in the report; nine with severe polyarthritis who recovered without relapse; nine who suffered one or more relapses and ten in whom the predominant feature was the cardiac involvement and belonging to the continuous type of the disease. In the absence of evidences of concomitant nonrheumatic infection, a persisting leucocytosis signified persistence of rheumatic infection and conversely repeated normal counts indicated that the attack was drawing to a close. This is particularly true if the patient is free from the influence of medication.

Another noteworthy point is that the leucocyte curves of patients with subcutaneous nodules, rheumatic carditis or the subacute relapsing type of polyarthritis was more markedly affected by drugs later in the disease than in the earlier months. In considering, therefore, the relation of the leucocyte curve to the type of the disease and to treatment, the period of infection, as well as the type of tissue response shown by the patient must be taken into account.

The differential formula has not proved to have any prognostic value. Only in patients with chorea or with erythema multiforme did the authors find an eosinophilia.

Patients in whom there are predominant exudative phenomena such as polyarthritis, pleurisy or pericarditis, together with high fever usually have a more marked leucocytosis than those in whom the tissue reaction is chiefly proliferative, such as is seen in myocarditis, endocarditis, or subcutaneous nodules.